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Directory of Clinics

FOR THE DIAGNOSIS AND TREATMENT OF VENEREAL DISEASES

Supplement No. 4 to Venereal Disease Information

Revised January 1, 1941

FEDERAL SECURITY AGENCY

PUBLIC HEALTH TERVICE

THOMAS PARRAN, *Surgeon General*

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THIS directory is for the information of health officers, physicians, nurses, and social workers in referring persons unable to pay for private care to public or semipublic medical agencies for the diagnosis and treatment of the venereal diseases.

The directory is recommended for use in clinics as an aid in the transfer of patients, and for all types of social welfare agencies whose clients may be in need of medical care for the venereal diseases.

The listing is by State and municipality. The name and address of the clinic is given, with information as to whether treatment is provided free or for a nominal charge, and what diseases are treated.

Unless otherwise specified, the clinics listed in this supplement provide both diagnostic and treatment services without regard to sex, race, or age of patient.

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ALABAMA

Abbeville, Henry Co.: Henry Co. Clinic, Health Office. Free; all venereal diseases.

Albertville, Marshall Co.: Marshall Co. Clinic, Courthouse. Free; all venereal diseases.

Alexander City, Tallapoosa Co.: Tallapoosa Co. Clinic, City Hall. Free; all venereal diseases.

Aliceville, Pickens Co.: Pickens Co. Clinic, City Hall. Free; all venereal diseases.

Andalusia, Covington Co.: Covington Co. Clinic, County Health Unit. Free, and part-pay; all venereal diseases.

Anniston, Calhoun Co.: Calhoun Co. Clinic, Courthouse Annex. Part-pay; all venereal diseases.

Ashland, Clay Co.: Clay Co. Clinic, Health Office, Courthouse Annex. Free; all venereal diseases.

Ashville, St. Clair Co.: St. Clair Co. Clinic, Health Office. Free; all venereal diseases.

Athens, Limestone Co.: Limestone Co. Clinic, Health Office, Browns Ferry St. Free; syphilis and gonorrhea only.

Atmore, Escambia Co.: Escambia Co. Clinic, Bank of Atmore Bldg. Free; all venereal diseases.

Auburn, Lee Co.: Lee Co. Clinic, Opelika Road. Free; syphilis and gonorrhea only.

Autaugaville, Autauga Co.:

Autauga Co. Clinic, Health Office. Free; all venereal diseases.

Mulberry Clinic. Free; all venereal diseases.

Bay Minette, Baldwin Co.: Baldwin Co. Clinic, Health Office. Free; all venereal diseases.

Bayou la Batre, Mobile Co.: Mobile Co. Clinic, Health Office. Free; all venereal diseases.

Bessemer, Jefferson Co.: Jefferson Co. Clinic, 1724 Third Ave. N. Free and part-pay; all venereal diseases.

Birmingham, Jefferson Co.:

Hillman Hospital, 620 South 20th St. Free and pay or part-pay; all venereal diseases.

Slossfield Clinic, 2501 19th St. N. (Negro only.) Part-pay; all venereal diseases.

Western Health Center, 2215 Ensley Ave. Part-pay; syphilis only.

Bleeker, Lee Co.: Lee Co. Clinic, Health Office. Free; syphilis and gonorrhea only.

Brewton, Escambia Co.: Escambia Co. Clinic, Health Office. Free; all venereal diseases.

Brownsville, Tuscaloosa Co.: Tuscaloosa Co. Clinic, Dr. Guin's Office. Free; all venereal diseases.

Butler, Choctaw Co.: Choctaw Co. Clinic, Health Office. Free; all venereal diseases.

Camden, Wilcox Co.: Wilcox Co. Clinic, Health Office. Free; all venereal diseases.

Carrollton, Pickens Co.: Pickens Co. Clinic, Health Office. Free; all venereal diseases.

Center, Cherokee Co.: Cherokee Co. Health Office, Courthouse. Free; all venereal diseases.

Centerville, Bibb Co.: Bibb Co. Clinic, Health Office, over Meigs' Drugstore. Free; all venereal diseases.

Chatom, Washington Co.: Washington Co. Clinic, Health Office. Free; all venereal diseases.

Childersburg, Talladega Co.: Talladega Co. Clinic, Health Office. Free; all venereal diseases.

Citronelle, Mobile Co.: Mobile Co. Clinic, Dr. Thompson's Office. Free; all venereal diseases.

Clanton, Chilton Co.: Chilton Co. Clinic, Health Office. Free; all venereal diseases.

Coffeeville, Clarke Co.: Clarke Co. Clinic, Health Office. Free; all venereal diseases.

Columbiana, Shelby Co.: Shelby Co. Clinic, Health Office, Main St. Free; all venereal diseases.

Courtland, Lawrence Co.: Lawrence Co. Clinic, Health Office. Free; all venereal diseases.

Cullman, Cullman Co.: Cullman Co. Clinic, Cullman Hospital. Free; all venereal diseases.

Dadeville, Tallapoosa Co.: Tallapoosa Co. Clinic, Health Office, Courthouse. Free; all venereal diseases.

Decatur, Morgan Co.: Morgan Co. Clinic, Health Office, 302 Second Ave. Free; all venereal diseases.

Demopolis, Marengo Co.: Marengo Co. Clinic, City Hall. Free; all venereal diseases.

Dothan, Houston Co.: Houston Co. Clinic, Health Office, 117½ North St. Free; all venereal diseases.

Double Springs, Winston Co.: Winston Co. Clinic, Health Office, Courthouse. Free; all venereal disease.

Elba, Coffee Co.: Coffee Co. Clinic, Courthouse. Free; syphilis only.

Enterprise, Coffee Co.: Coffee Co. Clinic, Health Office. Free; syphilis only.

Eutaw, Greene Co.: Greene Co. Clinic, Health Office. Free; all venereal diseases.

Evergreen, Conecuh Co.: Conecuh Co. Clinic, Health Office. Free; syphilis only.

Fairfax, Chambers Co.: Chambers Co. Clinic, Colored Health Center. Free; all venereal diseases.

Fairhope, Baldwin Co.: Baldwin Co. Clinic, Health Office. Free; all venereal diseases.

Fayette, Fayette Co.: Fayette Co. Clinic, Health Office, North Peyton St. (Courthouse Annex). Free; all venereal diseases.

Florala, Covington Co.: Covington Co. Clinic. Free; all venereal diseases.

Florence, Lauderdale Co.: Lauderdale Co. Clinic, Health Office, Court and Tennessee Streets. Free; all venereal diseases.

Ft. Deposit, Lowndes Co.: Lowndes Co. Clinic, Health Office. Free; syphilis only.

Fort Payne, DeKalb Co.: DeKalb Co. Clinic, Health Office, Courthouse Basement. Free; all venereal diseases.

Fruitdale, Washington Co.: Washington Co. Clinic. Free; all venereal diseases.

Geneva, Geneva Co.: Geneva Co. Clinic, Health Office, Academy St. Free; all venereal diseases.

Georgiana, Butler Co.: Butler Co. Clinic, Butler Co. Drugstore. Free; all venereal diseases.

Goodwater, Coosa Co.: Coosa Co. Clinic, Health Office. Free; syphilis only.

Greensboro, Hale Co.: Hale Co. Clinic, Health Office. Free; all venereal diseases.

Greenville, Butler Co.: Butler Co. Clinic, Health Office. Free; all venereal diseases.

Grove Hill, Clarke Co.: Clarke Co. Clinic, Health Office. Free; syphilis only.

Haleyville, Winston Co.: Winston Co. Clinic, City Hall, Main St. Free; all venereal diseases.

Hamilton, Marion Co.: Marion Co. Clinic, Health Office. Free; syphilis only.

Hayneville, Lowndes Co.: Lowndes Co. Clinic, Health Office. Free; syphilis only.

Headland, Henry Co.: Henry Co. Clinic, Health Center, City Hall. Free; all venereal diseases.

Heflin, Cleburne Co.: Cleburne Co. Clinic, Health Office. Free; all venereal diseases.

Huntsville, Madison Co.: Madison Co. Clinic, Courthouse Annex. Part pay; all venereal diseases.

Jacksonville, Calhoun Co.: Calhoun Co. Clinic, Health Office, City Hall. Free; all venereal diseases.

Jasper, Walker Co.: Walker Co. Clinic, Health Office, Courthouse. Free; all venereal diseases.

Lanett, Chambers Co.: Chambers Co. Clinic, Goodsell M. E. Church. Free; all venereal diseases.

Leighton, Colbert Co.: Colbert Co. Clinic, Over Model Drugstore. Free; all venereal diseases.

Livingston, Sumter Co.: Sumter Co. Clinic, Health Office. Free; all venereal diseases.

Loachapoka, Lee Co.: Lee Co. Clinic, Health Office. Free; syphilis and gonorrhea only.

Luverne, Crenshaw Co.: Crenshaw Co. Clinic, Health Office, City Hall. Free; all venereal diseases.

Maplesville, Chilton Co.: Chilton Co. Clinic, Health Office. Free; all venereal diseases.

Marion, Perry Co.: Perry Co. Clinic, Health Office. Free; all venereal diseases.

Midway, Bullock Co.: Bullock Co. Clinic, Health Office. Free; all venereal diseases.

Millport, Lamar Co.: Lamar Co. Clinic, Health Office. Free; all venereal diseases.

Minter, Dallas Co.: Dallas Co. Clinic, 109 Church St. Free; all venereal diseases.

Mobile, Mobile Co.: Mobile Co. Clinic, City Hospital, 850 St. Anthony St. Free; all venereal diseases.

Monroeville, Monroe Co.: Monroe Co. Clinic, Health Office. Free; all venereal diseases.

Montevallo, Shelby Co.: Shelby Co. Clinic, Fancher Bldg., Main St. Free; all venereal diseases.

Montgomery, Montgomery Co.:

Fraternal Hospital, 42 Dorsey St. (Negro only.) Free; syphilis only.

Montgomery Co. Clinic, City Hall. Free; all venereal diseases.

Moulton, Lawrence Co.: Lawrence Co. Clinic, Health Office. Free; all venereal diseases.

Moundville, Hale Co.: Hale Co. Clinic, Health Office. Free; all venereal diseases.

Mt. Vernon, Mobile Co.: Mobile Co. Clinic, Dr. Tisdale's Office. Free; all venereal diseases.

New Brocton, Coffee Co.: Coffee Co. Clinic, Health Office. Free; all venereal diseases.

Newville, Henry Co.: Henry Co. Clinic, Vacant Store. Free; all venereal diseases.

Oneonta, Blount Co.: Blount Co. Clinic, Health Office. Free; all venereal diseases.

Opelika, Lee Co.:

Lee Co. Clinic, Ninth St. and South R. R. Ave. Free; syphilis and gonorrhea only.

Marvyn Clinic, Route 2. Free; syphilis and gonorrhea only.

Opp, Covington Co.: Covington Co. Clinic, Health Office. Free; all venereal diseases.

Ozark, Dale Co.: Dale Co. Clinic, Health Office. Free; syphilis only.

Pell City, St. Clair Co.: St. Clair Co. Clinic, Courthouse. Free; all venereal diseases.

Phenix City, Russell Co.: Russell Co. Clinic, Health Office. Free; all venereal diseases.

Pittsview, Russell Co.: Russell Co. Clinic, Health Office. Free; all venereal diseases.

Prattville, Autauga Co.: Autauga Co. Clinic, Health Office. Free; all venereal diseases.

Prichard, Mobile Co.: Mobile Co. Clinic, City Hall Annex. Free; all venereal diseases.

Ragland, St. Clair Co.: St. Clair Co. Clinic, Health Office. Free; all venereal diseases.

Repton, Conecuh Co.: Conecuh Co. Clinic, Old Post Office Bldg. Free; syphilis only.

Roanoke, Randolph Co.: Randolph Co. Clinic, Branch Health Office. Free; syphilis only.

Rockford, Coosa Co.: Coosa Co. Clinic, Health Office. Free; syphilis only.

Russellville, Franklin Co.: Franklin Co. Clinic, Health Office. Free; all venereal diseases.

Scottsboro, Jackson Co.: Jackson Co. Clinic, Health Office. Free; all venereal diseases.

Seale, Russell Co.: Russell Co. Clinic, Health Office. Free; all venereal diseases.

Selma, Dallas Co.: Dallas Co. Clinic, Health Office, 109 Church St. Free; all venereal diseases.

Sheffield, Colbert Co.: Colbert Co. Clinic, Health Office. Free; all venereal diseases.

Silas, Choctaw Co.: Choctaw Co. Clinic, Health Office. Free; all venereal diseases.

Springville, St. Clair Co.: St. Clair Co. Clinic, Dr. Grasberger's Office. Free; all venereal diseases.

Stevenson, Jackson Co.: Jackson Co. Clinic, City Hall. Free; all venereal diseases.

Sulligent, Lamar Co.: Lamar Co. Clinic, Elm Street. Free; all venereal diseases.

Sylacauga, Talladega Co.: Talladega Co. Clinic, Health Office, Third and Norton Sts. Free; all venereal diseases.

Talladega, Talladega Co.: Talladega Co. Clinic, Health Office, Court and South Sts. Free; all venereal diseases.

Troy, Pike Co.: Pike Co. Clinic, Health Office, Church St. Free; all venereal diseases.

Tuscaloosa, Tuscaloosa Co.: Tuscaloosa Co. Clinic, Health Office, Greensboro Ave. and 6th St. Free; all venereal diseases.

Tuscumbia, Colbert Co.: Colbert Co. Clinic, Health Office, Sixth St. Free; all venereal diseases.

Tuskegee, Macon Co.:

Adams' Store Clinic, Mobile Unit. Free; all venereal diseases.
Armstrong Clinic, Mobile Unit. Free; all venereal diseases.
Brownville Clinic, Mobile Unit. Free; all venereal diseases.
Carr's Store Clinic, Mobile Unit. Free; all venereal diseases.
Chesson Clinic, Mobile Unit. Free; all venereal diseases.
Creek Stand Clinic, Mobile Unit. Free; all venereal diseases.
Cross Roads Clinic, Mobile Unit. Free; all venereal diseases.
Downs Clinic, Mobile Unit. Free; all venereal diseases.
Ft. Davis Clinic, Mobile Unit. Free; all venereal diseases.
Hannon Clinic, Mobile Unit. Free; all venereal diseases.
Hadaway Clinic, Mobile Unit. Free; all venereal diseases.
James Station Clinic, Mobile Unit. Free; all venereal diseases.
Little Texas Clinic, Mobile Unit. Free; all venereal diseases.
Liverpool Clinic, Mobile Unit. Free; all venercal diseases.
Log Cabin Clinic, Mobile Unit. Free; all venereal diseases.
Macon Co. Clinic, Health Office. Free; all venereal diseases.
Milstead Clinic, Mobile Unit. Free; all venereal diseases.
Mt. Esther Clnic, Mobile Unit. Free; all venereal diseases.
Mt. Nebo Clinic, Mobile Unit. Free; all venereal diseases.
Mt. Pleasant Clinic, Mobile Unit. Free; all venereal diseases.
Mt. Zion Clinic, Mobile Unit. Free; all venereal diseases.
Pinkston's Store Clinic, Mobile Unit. Free; all venereal diseases.
Roba Clinic, Mobile Unit. Free; all venereal diseases.
St. Paul Clinic, Mobile Unit. Free; all venereal diseases.
Segrest Clinic, Mobile Unit. Free; all venereal diseases.
Shiloh Clinic, Mobile Unit. Free; all venereal diseases.
Society Hill Clinic, Mobile Unit. Free; all venereal diseases.
Swanson Clinic, Mobile Unit. Free; all venereal diseases.
Tysonville Clinic, Mobile Unit. Free; all venereal diseases.
Vine Bethel Clinic, Mobile Unit. Free; all venereal diseases.
Warrior Stand Clinic, Mobile Unit. Free; all venereal diseases.
White Church Clinic, Mobile Unit. Free; all venereal diseases.

Union Springs, Bullock Co.: Bullock Co. Clinic, Health Office. Free; all venereal diseases.

Uniontown, Perry Co.: Perry Co. Clinic, Health Office. Free; all venereal diseases.

Uriah, Monroe Co.: Monroe Co. Clinic. Free; all venereal diseases.

Vincent, Shelby Co.: Shelby Co. Clinic, Health Office. Free; all venereal diseases.

Wadley, Randolph Co.: Randolph Co. Clinic, Branch Health Office. Free; all venereal diseases.

Wedowee, Randolph Co.: Randolph Co. Clinic, Courthouse. Free; syphilis only.
West Blocton, Bibb Co.: Bibb Co. Clinic, Elks Home. Free; all venereal diseases.
Wetumpka, Elmore Co.: Elmore Co. Clinic, Courthouse, Commerce St. Free; all venereal diseases.
York, Sumter Co.: Sumter Co. Clinic, Health Office. Free; all venereal diseases.

ARIZONA

Bisbee, Cochise Co.: Cochise Co. Health Unit. Free; syphilis only.
Douglas, Cochise Co.: Cochise Co. Health Unit. Free; syphilis only.
Phoenix, Maricopa Co.:
Maricopa Co. Health Unit, 3 North 17th Ave. Free; all venereal diseases.
St. Monica Clinic, 809 South 7th Ave. (Negro only.) Free; syphilis only.
Social Service Center, Inc., 702 East Adams St. (White only.) Free; all venereal diseases.
Prescott, Yavapai Co.: Yavapai Co. Clinic, Room 2, Bashford Bldg. Free; all venereal diseases.
Tucson, Pima Co.:
Pima Co. Venereal Diseases Clinic—Syphilis, Room 14, Courthouse. Free; syphilis only.
Pima Co. Venereal Diseases Clinic—Gonorrhea, Courthouse. Free; gonorrhea only.
Winslow, Navajo Co.: Navajo Co. Clinic, Maternity Home. Part-pay; syphilis only.
Yuma, Yuma Co.: Yuma Co. Clinic, Courthouse. Free and part-pay; all venereal diseases.

ARKANSAS

Arkadelphia, Clark Co.: Clark Co. Health Unit, Courthouse. Free; syphilis only.
Ashdown, Little River Co.: Little River Co. Clinic, Courthouse. Free; syphilis only.
Augusta, Woodruff Co.: Woodruff Co. Clinic, Courthouse. Free; syphilis only.
Bald Knob, White Co.: White Co. Clinic, Front St. Free; all venereal diseases.
Batesville, Independence Co.: Independence Co. Health Unit, Barnett Bldg., Main St. Free; syphilis only.
Bauxite, Saline Co.: Saline Co. Health Unit, Mexican Camp. Free; all venereal diseases.
Benton, Saline Co.: Saline Co. Health Unit. Free; all venereal diseases.
Bentonville, Benton Co.: Benton Co. Clinic, Courthouse. Free; all venereal diseases.
Blytheville, Mississippi Co.: Mississippi Co. Health Unit, Courthouse. Free; syphilis only.
Brinkley, Monroe Co.: Monroe Co. Clinic, City Hall. Free; syphilis only.
Clarendon, Monroe Co.: Monroe Co. Clinic, Courthouse. Free; syphilis only.
Clarksville, Johnson Co.: Johnson Co. Health Unit, Courthouse. Free; syphilis only.
Clinton, Van Buren Co.: Van Buren Co. Clinic, Courthouse. (White only.) Free; syphilis only.
Conway, Faulkner Co.: Faulkner Co. Health Unit, U. S. Post Office Bldg. Free; all venereal diseases.

Crigler, Lincoln Co.: Lincoln Co. Health Unit (Cole Spur). Free; all venereal diseases.

Dardanelle, Yell Co.: Yell Co. Clinic, Courthouse. Free; all venereal diseases.

Elaine, Phillips Co.: Phillips Co. Clinic, Health Office. Free; syphilis only.

Eureka Springs, Carroll Co.: Carroll Co. Clinic, Courthouse. Free; syphilis only.

Fayetteville, Washington Co.: Washington Co. Clinic, Courthouse. Free; syphilis only.

Forrest City, St. Francis Co.: St. Francis Co. Health Unit, Courthouse. Free; syphilis only.

Fort Smith, Sebastian Co.: Sebastian Co. Health Unit, Welfare Bldg. Free; all venereal diseases.

Garland City, Miller Co.: Miller Co. Health Unit, Lowes Farm. Free; all venereal diseases.

Gurdon, Clark Co.: Clark Co. Health Unit. Free; syphilis only.

Hamburg, Ashley Co.: Ashley Co. Health Unit, Courthouse. Free; all venereal diseases.

Harrison, Boone Co.: Boone Co. Health Unit, Courthouse. Free; all venereal diseases.

Helena, Phillips Co.: Phillips Co. Mobile Unit, Courthouse. Free; syphilis only.

Holly Grove, Monroe Co.: Monroe Co. Health Unit, City Hall. Free; syphilis only.

Hope, Hempstead Co.: Hempstead Co. Health Unit, Courthouse. Free; syphilis only.

Hot Springs, Garland Co.:

Charles Steinberg Clinic, Levi Memorial Hospital, Prospect Ave. Free; all venereal diseases.

U. S. Public Health Service Clinic, Spring St. Free; all venereal diseases.

Hughes, St. Francis Co.: St. Francis Co. Health Unit. Free; syphilis only.

Jonesboro, Craighead Co.: Craighead Co. Health Unit, Courthouse. Free; all venereal diseases.

Laconia, Desha Co.: Desha Co. Mobile Unit, Snow Lake. Free; syphilis only.

Lake View, Phillips Co.: Phillips Co. Mobile Unit (Resettlement). Free; syphilis only.

Little Rock, Pulaski Co.:

Valley Grove-Baucum Clinic, Memphis Highway, Route #1. Free; all venereal diseases.

City Health Department Clinic, City Hall, Broadway & Markham St. Free; syphilis only.

Isaac Folsom Clinic, 12th and McAlmot Sts. Free; all venereal diseases.

Pulaski Co. Health Unit, Courthouse. Free; all venereal diseases.

Malvern, Hot Springs Co.: Hot Springs Co. Health Unit. Free; all venereal diseases.

Marianna, Lee Co.:

Lee Co. Mobile Unit, Chestnut St. Free; syphilis only.

Lee Co. Mobile Unit, Polk's Plantation, Route 1. Free; syphilis only.

Marion, Crittenden Co.: Crittenden Co. Health Unit. Free; all venereal diseases.

Marshall, Searcy Co.: Searcy Co. Health Unit, Adams Bldg. Free; syphilis only.

Marvell, Phillips Co.: Phillips Co. Mobile Unit. Free; syphilis only.

Mellwood, Phillips Co.: Phillips Co. Health Unit. Free; syphilis only.

Arkansas

Monticello, Drew Co.: Drew Co. Health Unit, Courthouse. Free; all venereal diseases.

Moro, Lee Co.: Lee Co. Mobile Unit, Courthouse. Free; syphilis only.

Morrilton, Conway Co.: Conway Co. Health Unit, Courthouse. Free; all venereal diseases.

Newport, Jackson Co.: Jackson Co. Health Unit, Courthouse. Free; all venereal diseases.

North Little Rock, Pulaski Co.: North Little Rock City Clinic, 116 East 3rd St. Free; all venereal diseases.

Okolona, Clark Co.: Clark Co. Health Unit. Free; syphilis only.

Osceola, Mississippi Co.: Mississippi Co. Health Unit, Courthouse. Free; syphilis only.

Ozark, Franklin Co.: Franklin Co. Health Department, Courthouse. Free; syphilis only.

Paragould, Green Co.: Green Co. Health Unit, W. Emerson St. Free; syphilis only.

Paris, Logan Co.: Logan Co. Health Unit, Courthouse. Free; syphilis only.

Piggott, Clay Co.: Clay Co. Health Unit, Bank Bldg. Free; syphilis only.

Plumerville, Conway Co.: Conway Co. Health Unit. Free; syphilis only.

Pocahontas, Randolph Co.: Randolph Co. Health Unit. Free; syphilis only.

Prescott, Nevada Co.: Nevada Co. Health Unit, City Hall. Free; all venereal diseases.

Rison, Cleveland Co.: Cleveland Co. Health Unit, Courthouse. Free; all venereal diseases.

Rogers, Benton Co.: Benton Co. Health Unit, City Hall. Free; all venereal diseases.

Russellville, Pope Co.: Pope Co. Health Unit, Courthouse. Free; all venereal diseases.

Searcy, White Co.: White Co. Health Unit, Courthouse. Free; all venereal diseases.

Siloam Springs, Benton Co.: Benton Co. Health Unit, Legion Hut. Free; all venereal diseases.

Simsboro, Crittenden Co.: Crittenden Co. Health Unit. Free; all venereal diseases.

Star City, Lincoln Co.: Lincoln Co. Health Unit. Free; all venereal diseases.

Texarkana, Miller Co.: Miller Co. Health Unit, Courthouse. Free; all venereal diseases.

Tongin, Lee Co.: Lee Co. Mobile Unit (rural), Brickey's Store. Free; syphilis only.

Walnut Ridge, Lawrence Co.: Lawrence Co. Health Unit, Lawrence Hotel Bldg. Free; syphilis only.

Warren, Bradley Co.: Bradley Co. Health Unit, 200½ Main St. Free; all venereal diseases.

West Memphis, Crittenden Co.: Crittenden Co. Health Unit. Free; all venereal diseases.

Wilmot, Ashley Co.: Ashley Co. Health Unit, City Hall. Free; all venereal diseases.

Winchester, Drew Co.: Drew Co. Health Unit, High School. Free; all venereal diseases.

Wynne, Cross Co.: Cross Co. Health Unit. Free; syphilis only.

Yellville, Marion Co.: Marion Co. Health Unit, Courthouse. Free; all venereal diseases.

CALIFORNIA

Alhambra, Los Angeles Co.: Health Center, 612 West Shorb St. Free; all venereal diseases.

Altadena, Los Angeles Co.: Health Center, 331 Crosby St. Free; all venereal diseases.

Arvin, Kern Co.: Venereal Disease Clinic. Free; all venereal diseases.

Atascadero, San Luis Obispo Co.: Atascadero General Hospital. Free; all venereal diseases.

Azusa, Los Angeles Co.: Health Center, 160 Azusa St. Free; all venereal diseases.

Bakersfield, Kern Co.: Kern Co. General Hospital. Free; all venereal diseases.

Banning, Riverside Co.: City Hall. Free; all venereal diseases.

Beaumont, Riverside Co.: 102 E. 5th St. Free; all venereal diseases.

Berkeley, Alameda Co.:

Berkeley Hospital, 2001 Dwight Way. Part-pay; all venereal diseases.

Cowell Hospital. (Private Hospital; University students only.) Free; all venereal diseases.

Blythe, Riverside Co.: Blythe Hospital. Free; all venereal diseases.

Brawley, Imperial Co.: Brawley Clinic. Free; all venereal diseases.

Broderick, Yolo Co.: Broderick Clinic, 5th and E Sts. Free; all venereal diseases.

Burbank, Los Angeles Co.: Health Center, 528 North Olive St. Free; all venereal diseases.

Burlingame, San Mateo Co.: Burlingame District Clinic, 248 Lorton Ave. Free; all venereal diseases.

Buttonwillow, Kern Co.: Venereal Disease Clinic. Free; all venereal diseases.

Calexico, Imperial Co.: Calexico Clinic. Free; all venereal diseases.

Carpinteria, Santa Barbara Co.: Carpinteria Health Center, Veterans Memorial Bldg. Free; all venereal diseases.

Chico, Butte Co.: Chico Health Center, 246 Salem St. Free; all venereal diseases.

Chino, San Bernardino Co.: Camp Chino Clinic. Free; syphilis only.

Colusa, Colusa Co.: Colusa Co. Hospital. Free; all venereal diseases.

Compton, Los Angeles Co.: Health Center, 1301 Willowbrook Ave. Free; all venereal diseases.

Corning, Tehama Co.: County Clinic, Dr. Arthur Henry Meuser's Office, Fourth Ave. Free; all venereal diseases.

Crescent City, Del Norte Co.: County Clinic, Dr. F. M. Stump's Office, 550 H St. Free, pay and part-pay; all venereal diseases.

Daly City, San Mateo Co.: Daly City District Clinic. Free; all venereal diseases.

Delano, Kern Co.: Venereal Disease Clinic. Free; all venereal diseases.

Dinuba, Tulare Co.: Tulare Co. Health Department, V. D. Clinic, 153 West Tulare St. Free; all venereal diseases.

East Los Angeles, Los Angeles Co.: Health Center, 670 South Ferris St. Free; all venereal diseases.

El Centro, Imperial Co.: El Centro Clinic, Courthouse. Free; all venereal diseases.

Eldridge, Sonoma Co.: Sonoma State Home. Free; all venereal diseases.

El Monte, Los Angeles Co.:

Health Center, 333 California St. Free; all venereal diseases.

Ruth Home Hospital. Free, and pay or part-pay; all venereal diseases.

Eureka, Humboldt Co.: Humboldt Co. Hospital. Free; all venereal diseases.

Fairfield, Solano Co.: Solano Co. Health Department. Free; all venereal diseases.

Farley, Mendocino Co.: State Relief Association, Camp Eel River. Free, and part-pay; syphilis only.

Fresno, Fresno Co.:

Fresno City Clinic, 1039 H St. Free; all venereal diseases.

Fresno County Hospital, 4461 Ventura Ave. Free; all venereal diseases.

Gilroy, Santa Clara Co.: County Health Department. Free; all venereal diseases.

Glendale, Los Angeles Co.: Health Center, 200 West Lexington Drive. Free; all venereal diseases.

Grass Valley, Nevada Co.:

Nevada Co. Clinic, 255 South Auburn St. Free; all venereal diseases.

Receiving Hospital, 118 Bush St. Pay and part-pay; all venereal diseases.

Gridley, Butte Co.: Gridley Clinic, office of Dr. H. T. Carey, 576 Kentucky St. Free; all venereal diseases.

Guadalupe, Santa Barbara Co.: Guadalupe Clinic, 302 Olivera St. Free, and pay or part-pay; all venereal diseases.

Half Moon Bay, San Mateo Co.: Half Moon Bay District Clinic, Dr. Borley's office. Free; all venereal diseases.

Hanford, Kings Co.: Kings Co. Hospital, Route 2. Free; all venereal diseases.

Healdsburg, Sonoma Co.: Sonoma Co. Clinic, 415 Center St., Recreation Hall. Free; all venereal diseases.

Huntington Park, Los Angeles Co.: San Antonio Health Center, 7300 Santa Fe Ave. Free; all venereal diseases.

Indio, Riverside Co.: Health Center. Free; all venereal diseases.

Inglewood, Los Angeles Co.: Health Center, 101 South Grevillea St. Free; all venereal diseases.

Ione, Amador Co.: Preston School of Industry Hospital. (Male only.) Free; all venereal diseases.

Jolon, Monterey Co.: Camp Nacimiento. Free; syphilis only.

King City, Monterey Co.: King City Clinic. Free; all venereal diseases.

Lancaster, Los Angeles Co.: Health Center, 311 West 10th St. Free; all venereal diseases.

Lompoc, Santa Barbara Co.: Lompoc Clinic, 122 North H St. Free and part-pay; all venereal diseases.

Loma Linda, San Bernardino Co.: Loma Linda Dispensary. Part-pay; all venereal diseases.

Long Beach, Los Angeles Co.: Long Beach Health Department Clinic, 404 City Hall. Free; all venereal diseases.

Los Angeles, Los Angeles Co.:

Children's Hospital, 4614 Sunset Blvd. (Children only.) Free and part-pay; syphilis only.

Good Hope Clinic, 1241 Shatto St. Part-pay; syphilis only.

Graves Memorial Dispensary, 737 North Broadway. Pay and part-pay; all venereal diseases.

Los Angeles Co. General Hospital, 1200 North State St. Free and part-pay; syphilis only.

Los Angeles Osteopathic Hospital, 1100 North Mission Road. Free and part-pay; syphilis only.

Los Angeles, Los Angeles Co.—Continued.

Men's Central Clinic, 116 Temple St., Room 200. (Male only.) Free; all venereal diseases.

West Los Angeles Clinic, 1620 Purdue Ave. Free; all venereal diseases.

White Memorial Clinic, 312 North Boyle Ave. Part-pay; all venereal diseases.

Women's Central Clinic, 116 West Temple St. (Female only.) Free; all venereal diseases.

Los Molinos, Tehama Co.: County Clinic, Dr. John H. Belyea's Office. Free; all venereal diseases.

Madera, Madera Co.: Madera Co. Hospital, Route 2. Free and pay or part-pay; all venereal diseases.

Martinez, Contra Costa Co.:

Contra Costa Co. Hospital. Free; all venereal diseases.

Martinez Health Department. Free; syphilis only.

Marysville, Yuba Co.: Sutter-Yuba Clinic, 309 C St. Free; all venereal diseases.

Merced, Merced Co.: General Hospital. Free and part-pay; all venereal diseases.

Modesto, Stanislaus Co.: County Hospital. Free and part-pay; all venereal diseases.

Monterey, Monterey Co.: Monterey Clinic, Abrego and Webster Sts. Free; all venereal diseases.

Monrovia, Los Angeles Co.: Health Center, 211 West Colorado Blvd. Free; all venereal diseases.

Montebello, Los Angeles Co.: Simons Clinic, Simons Brickyard. Free; all venereal diseases.

Oakland, Alameda Co.:

Children's Hospital of East Bay, 5105 Dover St. Part-pay; all venereal diseases.

Oakland City Clinic, 282 Eighth St. Free; all venereal diseases.

Pacific Protective Society, 2118 East 21st St. Part-pay; all venereal diseases.

Oroville, Butte Co.:

Butte Co. Hospital. Free; all venereal diseases.

Oroville Co. Clinic, 1453 Myers St., Dr. Ben C. Eperson's Office. Free; all venereal diseases.

Orange, Orange Co.: Orange Co. Clinic, Route 2. Free; all venereal diseases.

Pacoima, Los Angeles Co.: Pacoima Venereal Disease Clinic, 13133 Van Nuys Blvd. Free; all venereal diseases.

Paradise, Butte Co.: Paradise Clinic, Olive St., Office of Dr. Dorothy Lord. Free; all venereal diseases.

Pasadena, Los Angeles Co.: Pasadena Health Department, 38 Congress St. Free and part-pay; all venereal diseases.

Paso Robles, San Luis Obispo Co.: County Clinic. Free; all venereal diseases.

Pescadero, San Mateo Co.: Pescadero Clinic, Dr. C. V. Thompson's Office. Free; all venereal diseases.

Petaluma, Sonoma Co.: Sonoma Co. Clinic, 17 Fourth St. Free; all venereal diseases.

Pittsburg, Contra Costa Co.: Pittsburg City Clinic, 263 East 8th St. Free; all venereal diseases.

Pomona, Los Angeles Co.: Health Center, 280 West Fifth St. Free; all venereal diseases.

Quincy, Plumas Co.: Plumas Co. Hospital. Free; all venereal diseases.

Red Bluff, Tehama Co.: County Clinic, 410 Pine St. Free; all venereal diseases.

Redding, Shasta Co.: Shasta Co. Hospital. Free; all venereal diseases.

Redwood City, San Mateo Co.: Redwood City District Clinic, Courthouse. Free; all venereal diseases.

Richmond, Contra Costa Co.: Contra Costa Co. Health Clinic, 240 Eighth St. Free; all venereal diseases.

Sacramento, Sacramento Co.:

Sacramento Co. Hospital, Stockton Blvd. Free; syphilis only.

Sacramento Municipal Clinic, 504 I St. Free; all venereal diseases.

State Relay Association, Camp Natoma Clinic. Free; syphilis only.

Salinas, Monterey Co.: Monterey Co. Hospital. Free; all venereal diseases.

San Bernardino, San Bernardino Co.: County Health Center, 236 Fourth St. Free; all venereal diseases.

San Diego, San Diego Co.: Municipal Clinic, Civic Center. Free; all venereal diseases.

San Fernando, Los Angeles Co.: Health Center, 604 Maclay Ave. Free; all venereal diseases.

San Francisco, San Francisco Co.:

Children's Hospital, 3700 California St. Free and part-pay; all venereal diseases.

Homeopathic Clinic, 129 Haight St. Free and part-pay; all venereal diseases.

Mount Zion Clinic, 2200 Post St. Free and pay or part-pay; all venereal diseases.

San Francisco Health Department Clinic, 33 Hunt St. Free; all venereal diseases.

San Francisco Polyclinic and Post Graduate College, 1535 Jackson St. Part-pay; all venereal diseases.

St. Luke's Hospital, 27th and Valencia Sts. (Adults only.) Free and part-pay; syphilis only.

Stanford University Hospital, 2398 Sacramento St. Free and pay or part-pay; all venereal diseases.

University of California Out-patient Department, 2nd and Parnassus Ave. Free and pay or part-pay; all venereal diseases.

San Jacinto, Riverside Co.: Health Center. Free; all venereal diseases.

San Jose, Santa Clara Co.:

Jackson Ave. Clinic. Free; all venereal diseases.

Santa Clara Co. Health Department, Hall of Justice. Free; all venereal diseases.

Santa Clara Co. Hospital. Free; all venereal diseases.

San Leandro, Alameda Co.: Fairmont Clinic. Free; syphilis only.

San Luis Obispo, San Luis Obispo Co.: County Health Department, 1009 Morro St. Free; all venereal diseases.

San Mateo, San Mateo Co.: Community Hospital. Free; all venereal diseases.

San Pedro, Los Angeles Co.: San Pedro City Clinic, 599 West Seventh St. Free; all venereal diseases.

Santa Barbara, Santa Barbara Co.: Santa Barbara Health Center, 507 Santa Barbara St. Free; all venercal diseases.

Santa Cruz, Santa Cruz Co.: Emeline St. Free; all venereal diseases.

Santa Margarita, San Luis Obispo Co.: Santa Margarita Clinic, C. R. A. Camp. Free; all venereal diseases.

Santa Maria, Santa Barbara Co.: Santa Maria Hospital, Parkview St. Free; all venereal diseases.

Santa Monica, Los Angeles Co.: Health Center, 1525 Euclid St. Free; all venereal diseases.

Santa Rosa, Sonoma Co.:

Sonoma Co. Health Department, 505 B St. Free; all venereal diseases.

Sonoma Co. Jail Clinic. (Adults only.) Free; all venereal diseases.

Sebastopol, Sonoma Co.: Sonoma Co. Health Department, Sheridan Lane (old house back of Safeway Ave.). Free; all venereal diseases.

Shasta Dam, Shasta Co.: Shasta Dam Hospital. Pay and part-pay; all venereal diseases.

Sonoma, Sonoma Co.: Sonoma County Health Department, City Hall. Free; all venereal diseases.

Sonora, Tuolumne Co.: Tuolumne Co. Clinic. Free; all venereal diseases.

Stockton, San Joaquin Co.:

San Joaquin Local Health District, V. D. Clinic, 130 South American St. Free; all venereal diseases.

Stockton State Hospital. Free and pay; neurosyphilis and mental cases with coincident syphilis.

Stockton Project Clinic (State Relief Camp, French Camp). (Men only.) Free; all venereal diseases.

Taft, Kern Co.: Venereal Disease Clinic. Free; all venereal diseases.

Torrance, Los Angeles Co.: Health Center, 2300 Carson St. Free; all venereal diseases.

Tulare, Tulare Co.: Tulare Co. General Hospital. Free; all venereal diseases.

Ukiah, Mendocino Co.: County Clinic, Office of Dr. H. O. Clelland. Pay and part-pay; all venereal diseases.

Vallejo, Solano Co.: County Clinic, Health Department. Free; all venereal diseases.

Van Nuys, Los Angeles Co.: Van Nuys V. D. Clinic, 14410 Sylvan St. (Valley Municipal Bldg.) Corner Sylvan and Sylmar Sts. Free; all venereal diseases.

Venice, Los Angeles Co.: Venice V. D. Clinic, 685 Venice Blvd. Free; all venereal diseases.

Ventura, Ventura Co.:

Ventura City Health Department, 121 North Fir St. Free; all venereal diseases.

Ventura Co. Clinic, Loma Vista Road. Free and part-pay; all venereal diseases.

Ventura School for Girls. (Female only.) Free; all venereal diseases.

Visalia, Tulare Co.: County Health Department, 1501 West Main St. Free; all venereal diseases.

Watts, Los Angeles Co.:

Watts V. D. Clinic for Men, City Hall. Free; all venereal diseases.

Watts V. D. Clinic for Women, 1513 East 103d St. (Boys up to 12 years admitted.) Free; all venereal diseases.

West Hollywood, Los Angeles Co.: Health Center, 730 North San Vicente Blvd. Free; all venereal diseases.

Whittier, Los Angeles Co.: Health Center, 402 South Greenleaf St. Free; all venereal diseases.

Williams, Colusa Co.: Williams Clinic, Office of Dr. Charles M. Keith. Free and part-pay; all venereal diseases.

Willows, Glenn Co.: Glenn Co. Hospital. Free; all venereal diseases.

Wilmington, Los Angeles Co.: County Clinic, 212 F St. Free; all venereal diseases.

Woodland, Yolo Co.: Yolo Co. Hospital. Free; all venereal diseases.

Yreka, Siskiyou Co.:

Yreka Co. Clinic, 303 North Oregon St. Pay and part-pay; all venereal diseases.

Yreka Co. Hospital. Free; all venereal diseases.

COLORADO

Colorado Springs, El Paso Co.: El Paso Co. Public Health Clinic, 28 East Boulder St. Free; all venereal diseases.

Denver, Denver Co.:

Denver Co. Clinic, University of Colorado School of Medicine, 4200 East 9th Ave. Free; syphilis only.

Denver Co. Health Clinic, General Hospital. Free; all venereal diseases.

Fort Collins, Larimer Co.: Larimer Co. Public Health Clinic, Rohling Bldg., 125 Linden St. Free; all venereal diseases.

Fowler, Otero Co.: Otero Co. Health Department. Free; all venereal diseases.

Greeley, Weld Co.: Weld Co. Public Health Clinic, 1528 11th Ave. Free; all venereal diseases.

La Junta, Otero Co.: Otero Co. Health Department, 17 West 4th St. Free; all venereal diseases.

Manzanola, Otero Co.: Otero Co. Health Department. Free; all venereal diseases.

Pueblo, Pueblo Co.: Pueblo Co. Public Health Clinic, City Hall. Free; all venereal diseases.

Rocky Ford, Otero Co.: Otero Co. Public Health Clinic, 9th and Walnut Sts. Free; all venereal diseases.

CONNECTICUT

Bethel, Fairfield Co.: Treatment Station, 155 Greenwood Ave., Office of Dr. A. J. Trimpert. Free; syphilis only.

Branford, New Haven Co.: Treatment Station, 87 Main St., Office of Dr. Dana L. Blanchard. Free; syphilis only.

Bridgeport, Fairfield Co.: Welfare Bldg., Washington and Madison Aves. Part-pay; all venereal diseases.

Bristol, Hartford Co.: 110 South St. Free; all venereal diseases.

Broad Brook, Hartford Co.: Treatment Station, Office of Dr. W. C. Robinson. Free; syphilis only.

Canaan, Litchfield Co.: Treatment Station, Main St., Office of Dr. John R. Elliott. Free; syphilis only.

Cheshire, New Haven Co.: Treatment Station, Main St., Office of Dr. W. J. Moore. Free; syphilis only.

Clinton, Middlesex Co.: Treatment Station, 49 Pearl St., Office of Dr. Norman P. Rindge. Free; syphilis only.

Cornwall Bridge, Litchfield Co.: Treatment Station, Warren Road, Office of Dr. Joseph Evarts. Free; syphilis only.

Danbury, Fairfield Co.: Treatment Station, 158 Deer Hill Ave., Office of Dr. William A. Sunderland. Free; syphilis only.

Danielson, Windham Co.: Treatment Station, 7 Broad St., Office of Dr. Cecil R. Garcin. Free; syphilis only.

Darien, Fairfield Co.: Treatment Station, 166 Post Road, Office of Dr. William H. Slaughter. Free; syphilis only.

Deep River, Middlesex Co.: Treatment Station, 25 Elm St., Office of Dr. W. J. Tate. Free; syphilis only.

Derby, New Haven Co.: Treatment Station, 18 Elizabeth St., Office of Dr. Thomas F. Plunkett. Free; syphilis only.

East Hartford, Hartford Co.: Treatment Station, 27 Wells Ave., Office of Dr. F. W. Becker. Free; syphilis only.

Essex, Middlesex Co.: Treatment Station, New City St., Office of Dr. J. C. Scott. Free; syphilis only.

Fairfield, Fairfield Co.: Treatment Station, 133 Reef Road, Office of Dr. S. L. Biehn. Free; syphilis only.

Farmington, Hartford Co.: Treatment Station, Elm Tree Inn, Office of Dr. Francis D. Ellis. Free; syphilis only.

Granby, Hartford Co.: Treatment Station, Office of Dr. E. R. Pendleton. Free; syphilis only.

Greenwich, Fairfield Co.:

Greenwich Hospital Association, William St. Free; syphilis only.

Municipal Hospital, Parsonage Road. Free; all venereal diseases.

Groton, New London Co.: Treatment Station, 242 Thames St., Office of Dr. C. T. Hewes. Free; syphilis only.

Hampton, Windham Co.: Treatment Station, Main St., Office of A. D. Marsh. Free; syphilis only.

Hartford, Hartford Co.:

Board of Health Clinic, 39 Arch St. Free; all venereal diseases.

Dispensary, 56 Winthrop St. Part-pay; all venereal diseases.

Municipal Hospital, 4 Holcomb St. Free; syphilis only.

St. Francis Hospital, 370 Collins St. Part-pay; syphilis only.

Litchfield, Litchfield Co.: Treatment Station, 80 West St., Office of Dr. J. F. Kilgus, Jr. Free; syphilis only.

Manchester, Hartford Co.: Treatment Station, 689 Main St., Office of Dr. D. C. Y. Moore. Free; syphilis only.

Meriden, New Haven Co.: County Clinic, 181 Cook Ave. Free; syphilis only.

Middletown, Middlesex Co.:

Treatment Station, 28 Crescent St. Free; syphilis only.

Venereal Disease Clinic, 51 Broad St. Free; all venereal diseases.

Naugatuck, New Haven Co.: Treatment Station, 83 Meadows St., Office of Dr. Vincent Duffy. Free; syphilis only.

New Britain, Hartford Co.: Board of Health Clinic, General Hospital, 92 Grand St. Free (fee for out-of-town patients); all venereal diseases.

New Canaan, Fairfield Co.: Treatment Station, 80 South Ave., Office of Dr. Oswald D. Cammann. Free; syphilis only.

New Hartford, Litchfield Co.: Treatment Station, 14 Main St., Office of Dr. Homer Ashley. Free; syphilis only.

New Haven, New Haven Co.:

Urological Clinic, Grace Hospital, 1418 Chapel St. (Adults only.) Free; gonorrhea only.

Pediatric Clinic, Grace Hospital, 1418 Chapel St. (Children only.) Free: syphilis only.

Municipal Clinic, 106 William St. Part-pay; all venereal diseases.

Special Pediatric Clinic, New Haven Hospital Dispensary, 789 Howard Ave. (Children only.) Free; all venereal diseases.

Special Medical Clinic, New Haven Hospital Dispensary, 789 Howard Ave. (Adults only.) Free; all venereal diseases.

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Newington, Hartford Co.: Treatment Station, 866 Main St., Office of Dr. Theodore Sills. Free; syphilis only.

New London, New London Co.: County Clinic, 116 Huntington St. Free; all venereal diseases.

New Milford, Litchfield Co.: Treatment Station, 50 Bridge St., Office of Dr. Howard G. Stevens. Free; syphilis only.

Newtown, Fairfield Co.: Treatment Station, Main St., Office of Dr. Waldo Desmond. Free; syphilis only.

Niantic, New London Co.: Treatment Station, 61 Main St., Office of Dr. F. B. Dart. Free; syphilis only.

Norfolk, Litchfield Co.: Treatment Station, Greenwoods Road West, Office of Dr. Frank D. Ursone. Free; syphilis only.

Norwalk, Fairfield Co.: County Clinic, 79 Washington St. Free; all venereal diseases.

Norwich, New London Co.: W. W. Backus Hospital, 326 Washington St. Free; all venereal diseases.

Old Lyme, New London Co.: Treatment Station, Main St., Office of Dr. E. K. Devitt. Free; syphilis only.

Pawcatuck, New London Co.: Treatment Station, 101 West Broad St., Office of Dr. Samuel S. Farago. Free; syphilis only.

Portland, Middlesex Co.: Treatment Station, 309 Main St., Office of Dr. Philip E. Schwartz. Free; syphilis only.

Putnam, Windham Co.: Treatment Station, 66 Main St., Office of Dr. Karl T. Phillips. Free; syphilis only.

Rockville, Tolland Co.: Treatment Station, 27 Park St., Office of Dr. Francis H. Burke. Free; syphilis only.

Simsbury, Hartford Co.: Treatment Station, Office of Dr. Owen L. Murphy, Free; syphilis only.

Southington, Hartford Co.: Treatment Station, Cor. Main and Center Sts., Office of Dr. E. M. Simmons. Free; syphilis only.

Stafford Springs, Tolland Co.: Treatment Station, 106 East Main St., Office of Dr. J. M. Givens. Free; syphilis only.

Stamford, Fairfield Co.: Stamford Hospital. Free; all venereal diseases.

Stratford, Fairfield Co.: Treatment Station, 1949 Main St., Office of Dr. Harold T. Oeseau. Free; syphilis only.

Suffield, Hartford Co.: Treatment Station, 339 Main St., Office of Dr. William Levy. Free; syphilis only.

Thompsonville, Hartford Co.: Treatment Station, 75 North Main St., Office of Dr. Frank F. Simonton. Free; syphilis only.

Torrington, Litchfield Co.: Treatment Station, 16 Litchfield St., Office of Dr. Frank L. Polito. Free; syphilis only.

Wallingford, New Haven Co.: 235 Center St. Free; syphilis only.

Waterbury, New Haven Co.:

Chase Memorial Dispensary, 43 Field St. Free; all venereal diseases.

St. Mary's Hospital, 56 Franklin St. Free; syphilis only.

Watertown, Litchfield Co.: Treatment Station, 429 Main St., Office of Dr. Edwin G. Reade. Free; syphilis only.

West Hartford, Hartford Co.: Treatment Station, 69 South Main St., Office of Dr. L. Q. Stewart. Free; syphilis only.

Westport, Fairfield Co.: Treatment Station, 44 Church Lane, Office of Dr. H. S. Phillips. Free; syphilis only.

Wethersfield, Hartford Co.: Treatment Station, 330 Main St., Office of Dr. Harold A. Howard. Free; syphilis only.

Willimantic, Windham Co.: Treatment Station, 672 Main St., Office of Dr. Reuben Rothblatt. Free; syphilis only.

Windsor, Hartford Co.: Treatment Station, 18 Elm St., Office of Dr. John M. Monacella. Free; syphilis only.

Windsor Locks, Hartford Co.: Treatment Station, 4 Oak St., Office of Dr. E. F. Carniglia. Free; syphilis only.

Winsted, Litchfield Co.: Treatment Station, 384 Main St., Office of Dr. Aaron Levy. Free; syphilis only.

Woodbury, Litchfield Co.: Treatment Station, Main St., Office of Dr. Howard S. Allen. Free; syphilis only.

DELAWARE

Dover, Kent Co.: State Board of Health Clinic, 320 West Division St. Free; all venereal diseases.

Frankford, Sussex Co.: State Board of Health Clinic, The Fire House. Free; all venereal diseases.

Georgetown, Sussex Co.: State Board of Health Clinic, The Circle. Free; all venereal diseases.

Middletown, New Castle Co.: State Board of Health, Old Academy Bldg., Main St. Free; all venereal diseases.

Milford, Sussex Co.: State Board of Health Clinic, 111 West 3d St. Free; all venereal diseases.

Newark, New Castle Co.: State Board of Health Clinic, East Main St. Free; all venereal diseases.

Rehoboth Beach, Sussex Co.: State Board of Health, Old School, Rehoboth Ave. (June to September only.) Free; all venereal diseases.

Seaford, Sussex Co.: State Board of Health Clinic, North and Poplar Sts. Free; all venereal diseases.

Smyrna, Kent Co.: State Board of Health Clinic, Welfare Home. Free; all venereal diseases.

Wilmington, New Castle Co.:

Delaware Hospital, 14th and Washington Sts. Part-pay; all venereal diseases.

Homeopathic Hospital, 1501 Van Buren St. Part-pay; all venereal diseases.

St. Francis Hospital, 8th and Clayton Sts. Part-pay; all venereal diseases.

State Board of Health, 301 Shipley St. (Negro only.) Free; all venereal diseases.

Wilmington General Hospital, Chestnut and Broom Sts. Part-pay; all venereal diseases.

DISTRICT OF COLUMBIA

Washington, D. C.:

Children's Hospital, 13th and W Sts., NW. (Children only.) Free and part-pay; all venereal diseases.

Columbia Hospital Clinic, 2425 L St., NW. (Women only.) Part-pay; all venereal diseases.

Emergency Hospital, 1711 New York Ave. Free and pay or part-pay; all venereal diseases.

Episcopal Hospital, 1147 Fifteenth St., NW. Part-pay; syphilis only.

Freedmen's Hospital, 6th and Bryant Sts., NW Free; all venereal diseases.

Washington, D. C.—Continued.

Gallinger Hospital, 19th and C Sts., SE. (Adults only.) Free; syphilis only.

Gallinger Hospital, 19th and C Sts., SE. (Women and children only.) Free; all venereal diseases.

Garfield Hospital, 11th St. and Florida Ave., NW. (Adults only.) Free and part-pay; all venereal diseases.

Georgetown University Hospital, 35th and N Sts., NW. Free and pay; all venereal diseases.

George Washington University Hospital, 1339 H St., NW. (Adults only.) Free and part-pay; all venereal diseases.

Maternal and Child Hygiene Center, Barrville School, Division and Hayes Sts., NE. (Women and children only.) Free; all venereal diseases.

Maternal and Child Hygiene Center, 301 G St., SW. (Women and ehildren only.) Free; all venereal diseases.

Maternal and Child Hygiene Center, 1364 Florida Ave., NE. (Women and children only.) Free; all venereal diseases.

Maternal and Child Hygiene Center, Weightman School 23d and M Sts., NW. (Women and ehildren only.) Free; all venereal diseases.

Maternal and Child Hygiene Center, 16 D St., NW. (Women and children only.) Free; all venereal diseases.

Maternal and Child Hygiene Center, 518 M St., NW. (Women and ehildren only.) Free; all venereal diseases.

Maternal and Child Hygiene Center, Third and G Sts., SE. (Women and ehildren only.) Free; all venereal diseases.

Maternal and Child Hygiene Center, Freedmen's Hospital, Sixth and Bryant Sts., NW. (Women and ehildren only.) Free; all venereal diseases.

Providence Hospital, 2d and D Sts., SE. Free and pay or part-pay; all venereal diseases.

Soeial Hygiene Clinic, 512 Eye St., NW. Free; all venereal diseases.

Southwest Health Center, Delaware Ave. and I St., SW. Free; all venereal diseases.

FLORIDA

Apalachicola, Franklin Co.: Franklin Co. Health Department. Part-pay; syphilis only.

Apopka, Orange Co.: Orange Co. Health Center. Free; syphilis only.

Avon Park, Highlands Co.: Highlands Co. Health Department. Free; all venereal diseases.

Baldwin, Duval Co.: Duval Co. Health Unit, Baldwin Colored Church. Free; all venereal diseases.

Bartow, Polk Co.: Polk Co. Hospital. Free; all venereal diseases.

Bayard, Duval Co.: Duval Co. Health Unit, Health Center. Free; all venereal diseases.

Belle Glade, Palm Beach Co.: Palm Beach Co. Health Department. Part-pay; all venereal diseases.

Boca Raton, Palm Beach Co.: Palm Beach Co. Health Department, City Hall. Part-pay; all venereal diseases.

Callahan, Nassau Co.: Nassau Co. Health Unit, Brades Store. Free; all venereal diseases.

Carrabelle, Franklin Co.: Franklin Co. Health Department. Free; syphilis only.

Century, Escambia Co.: Escambia Co. Health Department. Free; syphilis only.

Chattahoochee, Gadsden Co.: Florida State Hospital. (Patients of hospital only.) Free; syphilis only.

Clearwater, Pinellas Co.:

Pinellas Co. Health Unit, Health Center. (White only.) Free; syphilis only.

Pinellas Co. Health Unit, Health Center. (Negro only.) Free; syphilis only.

Clermont, Lake Co.: Lake Co. Health Department. Free; syphilis only.

Cottondale, Jackson Co.: Jackson Co. Health Department. Free; all venereal diseases.

Delray, Palm Beach Co.: Palm Beaeh Co. Clinic, Colored Schoolhouse. Part-pay; all venereal diseases.

Eustis, Lake Co.: Lake Co. Health Department, Health Center. Free; syphilis only.

Fernandina, Nassau Co.: Nassau Co. Health Unit. Free; all venereal diseases.

Fort Lauderdale, Broward Co.: Broward Co. Health Department, 501 South Andrews Avenue. Free; syphilis only.

Gainesville, Alachua Co.: City Health Department. Part-pay; syphilis only.

Gibson, Gadsden Co.: Gadsden Co. Clinic, Health Center. Free; syphilis only.

Graceville, Jackson Co.: Jackson Co. Health Department, Health Center. Free; all venereal diseases.

Greensboro, Gadsden Co.: Gadsden Co. Health Department, Health Center. Free; syphilis only.

Greenwood, Jackson Co.: Jaekson Co. Health Department, Health Center. Free; all venereal diseases.

Gretna, Gadsden Co.: Gadsden Co. Health Department, Health Center. Free; syphilis only.

Groveland, Lake Co.: Lake Co. Health Department. Free; syphilis only.

Havana, Gadsden Co.: Gadsden Co. Health Department, Health Center. Free; syphilis only.

Hilliard, Nassau Co.: Nassau Co. Health Department, over Leigh's Store. Free; all venereal diseases.

Hollywood, Broward Co.: Broward Co. Health Department, City Hall. Free; syphilis only.

Jacksonville, Duval Co.:

Duval Co. Health Unit, Beaeh Clinic, Colored Sehool. Free; all venereal diseases.

Brewster Hospital, 7th and Jefferson Sts. (Negro only.) Part-pay; all venereal diseases.

Duval Co. Health Unit, 205 East First St. Free; all venereal diseases.

Duval Co. Hospital, Duval-Jacksonville Demonstration Unit, 710 West 10th St. Free; syphilis and gonorrhea only.

Jasper, Hamilton Co.: Hamilton Co. Health Department. Free; syphilis only.

Key West, Monroe Co.: Monroe Co. Health Department, 1300 United St. Free; all venereal diseases.

Keysville, Hillsborough Co.: Hillsborough Co. Healthmobile, Commissary. Free; all venereal diseases.

Kissimmee, Osceola Co.: Oseeola Co. Health Department, Health Center. Free; all venereal diseases.

Lakeland, Polk Co.: Polk Co. Health Department, 809 North Kentueky Ave. Free; all venereal diseases.

Leesburg, Lake Co.: Lake Co. Health Department, Health Center. Free; syphilis only.

Marianna, Jackson Co.:

Jackson Co. Health Department. (White only.) Free; all venereal diseases.

Jackson Co. Health Department. (Negro only.) Free; all venereal diseases.

Macclenny, Baker Co.: Baker Co. Health Department. Free; syphilis only.

Miami, Dade Co.:

City Clinic, 910 Courthouse. Free and part-pay; all venereal diseases.

Dade Co. Hospital, Route 2. Free; all venereal diseases.

Molino, Escambia Co.: Escambia Co. Health Department, Health Center. Part-pay; all venereal diseases.

Moore Haven, Glades Co.: Glades Co. Health Department. Free; all venereal diseases.

Mount Dora, Lake Co.: Lake Co. Health Department. Free; syphilis only.

Orient Park, Hillsborough Co.: Hillsborough Co. Healthmobile, Carleton's Garage. Free; all venereal diseases.

Orlando, Orange Co.:

City Health Department, City Hall. Free and pay or part-pay; all venereal diseases.

County Clinic, 16 North Court St. Free and part-pay; all venereal diseases.

Pahokee, Palm Beach Co.: Palm Beach Co. Health Department. Part-pay; all venereal diseases.

Panama City, Bay Co.: Bay Co. Health Department, 546 Harrison Ave. Part-pay; all venereal diseases.

Pensacola, Escambia Co.:

Allen Chapel, 803 N. Palafox St. (Negro only.) Free; syphilis only.

City and County Jail, 803 N. Palafox St. (Adults only.) Free; all venereal diseases.

Escambia Co. Health Department, 803 N. Palafox St. Free; all venereal diseases.

Perry, Taylor Co.: Taylor Co. Health Department. Part-pay; all venereal diseases.

Plant City, Hillsborough Co.: Hillsborough Co. Healthmobile, Mays Bldg. Free; all venereal diseases.

Pompano, Broward Co.: Broward Co. Health Department, Clinic Bldg. Free; syphilis only.

Port St. Joe, Gulf Co.:

Gulf Co. Health Department, Kenney's Mill. Part-pay; syphilis only.

Gulf Co. Health Department. Free; syphilis only.

Punta Gorda, Charlotte Co.: Charlotte Co. Clinic. Free; syphilis only.

Quincy, Gadsden Co.: Gadsden Co. Health Department, Health Center. Free; syphilis only.

Raiford, Union Co.: Florida State Prison. Free; syphilis only.

River Junction, Gadsden Co.: Gadsden Co. Health Department, Health Center. Free; syphilis only.

Ruskin, Hillsborough Co.: Hillsborough Co. Healthmobile. Free; all venereal diseases.

St. Augustine, St. Johns Co.: Flagler Hospital, Tremerton St. Part-pay; syphilis only.

St. Petersburg, Pinellas Co.: City Health Department, 440 Second Ave. N. (White only.) Free; all venereal diseases.

Sebring, Highlands Co.: Highlands Co. Health Department. Free; all venereal diseases.

Shady Grove, Taylor Co.: Taylor Co. Health Department. Free; all venereal diseases.
Shamrock, Dixie Co.: Shamrock Hospital. Pay; all venereal diseases.
Sneads, Jackson Co.: Jackson Co. Health Department. Free; all venereal diseases.
Steinhatchee, Taylor Co.: Taylor Co. Health Department, Health Center. Free; all venereal diseases.
Sun City, Hillsborough Co.: Hillsborough Co. Healthmobile. Free; all venereal diseases.
Tallahassee, Leon Co.: Leon Co. Health Department, 323 East Gaines St. Free; syphilis only.
Tampa, Hillsborough Co.:
Healthmobile, 1301 Florida Ave. Free; all venereal diseases.
County Jail. Free; all venereal diseases.
Venereal Disease Clinic, 1420 Tampa St. Free; all venereal diseases.
Tarpon Springs, Pinellas Co.:
Pinellas Co. Health Department, Health Center, 1st National Bank Bldg. (White only.) Free; syphilis only.
Pinellas Co. Health Department, Health Center, 1st National Bank Bldg. (Negro only.) Free; syphilis only.
Taveres, Lake Co.: Lake Co. Health Department. Free; syphilis only.
Umatilla, Lake Co.: Lake Co. Health Department. Free; syphilis only.
Union Park, Orange Co.: Orange Co. Health Unit. Free; all venereal diseases.
Venus, Highlands Co.: Highlands Co. Health Department. Free; all venereal diseases.
Vero Beach, Indian River Co.: Indian River Co. (Fellsmere) Clinic, Arcade Bldg. (Negro only.) Part-pay; syphilis only.
West Palm Beach, Palm Beach Co.:
City Health Department, 5th and Railroad Sts. Free and part-pay; all venereal diseases.
West Palm Beach Syphilis Clinic, 902 Comeau Bldg. Part-pay; all venereal diseases.
Wewahitchka, Gulf Co.: Gulf Co. Health Department, Health Center. Free; syphilis only.
Wimauma, Hillsborough Co.: Hillsborough Co. Healthmobile, Health Center. Free; all venereal diseases.
Winter Garden, Orange Co.: Orange Co. Health Department, Health Center. Free; all venereal diseases.
Winter Park, Orange Co.: Orange Co. Health Department, Health Center, 104 East Park Ave. Free; all venereal diseases.
Yulee, Nassau Co.: Nassau Co. Health Department, Old Schoolhouse. Pay; all venereal diseases.

GEORGIA

Adairsville, Bartow Co.: County Clinic. Free; all venereal diseases.
Alamo, Wheeler Co.: Alamo Clinic. Free; syphilis only.
Albany, Dougherty Co.:
Albany Clinic. Free; syphilis only.
Albany (Congenital) Clinic. Free; syphilis only.
City Venereal Diseases Clinic, Broad St. Alley. Free; all venereal diseases.
Alma, Bacon Co.: Alma Clinic. Free; syphilis only.
Alpharetta, Fulton Co.: Alpharetta Health Center. Free; syphilis only.

Alto, Habersham Co.: Alto Clinic. Free; all venereal diseases.
Americus, Sumter Co.: Sumter Co. Health Department. Free; syphilis only.
Amsterdam, Decatur Co.: Amsterdam Clinic. Free; syphilis only.
Andersonville, Sumter Co.: Andersonville Clinic. Free; syphilis only.
Arlington, Calhoun Co.: Arlington Clinic. Free; syphilis only.
Athens, Clarke Co.: Clarke Co. Clinic, City Hall. Free; syphilis only.
Atlanta, Fulton Co.:
Dr. Dewell's Clinic. Free; syphilis only.
Georgia Baptist Hospital. Free; syphilis only.
Rockdale Park Health Center, Johnson Road. (Negro only.) Free; syphilis only.
Social Disease Hospital. Free; all venereal diseases.
Augusta, Richmond Co.: Richmond Co. Health Department, 501 Greene St. Free; syphilis only.
Bainbridge, Decatur Co.: Bainbridge Clinic. Free; syphilis only.
Barnesville, Lamar Co.: Lamar Co. Clinic. Free; syphilis only.
Blackshear, Pierce Co.: Blackshear Clinic. Free; all venereal diseases.
Blue Ridge, Fannin Co.: Venereal Disease Clinic. Free; syphilis only.
Bronwood, Terrell Co.: Bronwood Clinic, Terrell Co. Health Department. Free; syphilis only.
Brookfield, Tift Co.: Brookfield Clinic. Free; all venereal diseases.
Brooklet, Bulloch Co.: Brooklet Clinic. Free; syphilis only.
Brunswick, Glynn Co.:
Brunswick Clinic. Free; all venereal diseases.
Needwood Clinic, Mobile Unit, General Store. Free; all venereal diseases.
Burdal, Fulton Co.: Sandy Springs Health Center. Free; syphilis only.
Butler, Taylor Co.: Venereal Disease Clinic. Free; syphilis only.
Byron, Peach Co.: Peach Co. Clinic. Free; syphilis only.
Cairo, Grady Co.: Grady Co. Health Department. Free; all venereal diseases.
Camilla, Mitchell Co.: Camilla Clinic. Part-pay; syphilis only.
Carnesville, Franklin Co.: Carnesville Clinic. Free; syphilis and gonorrhea only.
Cartersville, Bartow Co.: Bartow Co. Clinic. Free; all venereal diseases.
Chamblee, De Kalb Co.: De Kalb Co. Board of Health, Office of Dr. A. I. Martin. Free; all venereal diseases.
Chattahoochee, Fulton Co.: Chattahoochee Clinic, Collins District Health Center. Free; syphilis only.
Chickamauga, Walker Co.: Chickamauga V. D. Clinic, Walker Co. Health Department. (Negro only.) Free; syphilis only.
Chipley, Harris Co.: Chipley Clinic. Free; syphilis only.
Chula, Tift Co.: Chula Clinic. Free; all venereal diseases.
Clarksville, Habersham Co.: Clarkesville Clinic. Free; all venereal diseases.
Clayton, Rabun Co.: Rabun Co. Clinic. Free; all venereal diseases.
Cochran, Bleckley Co.: Cochran Clinic. Free; syphilis only.
Columbus, Muscogee Co.:
City Hospital. Free; all venereal diseases.
County Jail. Free; all venereal diseases.
Cordele, Crisp Co.:
Cordele Clinic. Free; syphilis only.
Gillespie Hospital Clinic. Free; syphilis only.
Cornelia, Habersham Co.: Cornelia Clinic. Free; all venereal diseases.

Crescent, McIntosh Co.:
Crescent Clinic, Mobile Unit, Post Office. Free; all venereal diseases.
Cedar Point Clinic, Mobile Unit, Oyster Factory. Free; all venereal diseases.

Cuthbert, Randolph Co.: Cuthbert Clinic. Part-pay; all venereal diseases.

Dalton, Whitfield Co.: Whitfield Co. Health Department. Free; all venereal diseases.

Darien, McIntosh Co.:
Darien Clinic. Free; all venereal diseases.
Darien Clinic, Mobile Unit, Health Department. Free; all venereal diseases.

Dawson, Terrel Co.: Dawson Clinic, Terrel Co. Health Department. Free; syphilis only.

Decatur, De Kalb Co.: De Kalb Co. Clinic, 318 East Howard St. Free; all venereal diseases.

Doerun, Colquitt Co.: Doerun Clinic. Free; syphilis only.

Donalsonville, Seminole Co.: Donalson Clinic. Free; syphilis and gonorrhea only.

Douglas, Coffee Co.: Health Department. Free; all venereal diseases.

Eastman, Dodge Co.: Eastman Clinic. Free; syphilis and gonorrhea only.

East Point, Fulton Co.: East Point Health Center. Free; syphilis only.

Eatonton, Putnam Co.: Eatonton Clinic. Free; syphilis only.

Edison, Calhoun Co.: Edison Clinic. Free; syphilis only.

Eulonia, McIntosh Co.: Eulonia Clinic, Mobile Unit, Post Office. Free; all venereal diseases.

Everett City, Glynn Co.: Everett City Clinic, Mobile Unit, General Store. Free; all venereal diseases.

Fairburn, Fulton Co.: Fairburn Health Center. Free; syphilis only.

Fargo, Clinch Co.: Clinch Co. Clinic. Free; syphilis only.

Flint River, Macon Co.: Flint River Clinic. Part-pay; all venereal diseases.

Folkston, Charlton Co.:
Charlton Co. Clinic. (Negro only.) Free; syphilis only.
Silco Clinic, Mobile Unit, Schoolhouse. Free; all venereal diseases.

Ft. Valley, Peach Co.: Peach Co. Clinic. Free; syphilis only.

Forsyth, Monroe Co.: Hubbard Training School, Dr. L. T. Boddie's Office. (Negro children only.) Free; syphilis only.

Gainesville, Hall Co.: Gainesville Clinic. Free; all venereal diseases.

Gough, Burke Co.: Gough Clinic. Free; syphilis only.

Grantville, Coweta Co.: Grantville V. D. Clinic. Free; syphilis only.

Gray, Jones Co.: Jones Co. Clinic. Free; syphilis only.

Greensboro, Greene Co.: Greene Co. Clinic, Health Department. Free; syphilis only.

Greenville, Meriwether Co.: Greenville Clinic. Free; syphilis only.

Griffin, Spalding Co.: Syphilis Clinic, Courthouse. Free and part-pay; syphilis only.

Hamilton, Harris Co.: Hamilton Clinic. Free; syphilis only.

Hinesville, Liberty Co.: Hinesville Clinic. Free; syphilis only.

Hillsboro, Jasper Co.: Hillsboro Clinic, County Health Department. Free; all venereal diseases.

Homerville, Clinch Co.: Clinch Co. Health Department. Free; syphilis only.

Jackson, Butts Co.: Jackson Clinic. Free; syphilis only.

Jesup, Wayne Co.: Wayne Co. Department of Health. Free; syphilis only.

Kingsland, Camden Co.:
Gross' Turpentine Still Clinic, Mobile Unit. Free; all venereal diseases.
Kingsland Clinic, Mobile Unit, Schoolhouse. Free; all venereal diseases.

Kingston, Bartow Co.: Bartow Co. Clinic. Free; all venereal diseases.

Knoxville, Crawford Co.: Crawford Co. Clinic. Free; syphilis only.

La Fayette, Walker Co.: La Fayette V. D. Clinic, Walker Co. Health Department. Free; syphilis only.

La Grange, Troup Co.:
Callaway Mills Clinic. Free; syphilis only.
La Grange Clinic. Free; all venereal diseases.

Lakeland, Lanier Co.: Lakeland Clinic. Free; all venereal diseases.

Lavonia, Franklin Co.: Lavonia Clinic. Free; syphilis and gonorrhea only.

Leary, Calhoun Co.: Leary Clinic. Free; syphilis only.

Leesburg, Lee Co.: Venereal Disease Clinic. Free; syphilis only.

Lindale, Floyd Co.: Lindale Clinic. Free; syphilis only.

Louisville, Jefferson Co.: Louisville Clinic. Free; all venereal diseases.

Lithonia, De Kalb Co.: De Kalb Co. Board of Health, City Hall. Free; all venereal disease.

Ludowici, Long Co.: Ludowici Clinic. Free; syphilis only.

Lyons, Toombs Co.: Lyons Clinic, Toombs Co. Health Center. Free; all venereal diseases.

Macon, Bibb Co.: Macon Hospital, Pine St. Free and part-pay; all venereal diseases.

Manchester, Meriwether Co.: Manchester Clinic. Free; syphilis only.

Marshallville, Macon Co.: Marshallville Clinic. Free; syphilis only.

McDonough, Henry Co.: Henry Co. Clinic. Free; syphilis only.

McRae, Telfair Co.: Telfair Co. Health Department. Part-pay; all venereal diseases.

Meridian, McIntosh Co.: Meridian Clinic, Mobile Unit, Post Office. Free; all venereal diseases.

Metter, Candler Co.: Metter Clinic. Free; syphilis only.

Midville, Burke Co.: Midville Clinic. Free; all venereal diseases.

Milledgeville, Baldwin Co.: Baldwin Co. Health Department, Courthouse. Free; all venereal diseases.

Millen, Jenkins Co.: Venereal Disease Clinic, Jenkins Co. Health Department. Pay; syphilis only.

Monroe, Walton Co.: Walton Co. Health Department. Free; syphilis only.

Montezuma, Macon Co.: Montezuma Clinic. Free; syphilis only.

Monticello, Jasper Co.: Monticello Clinic, Courthouse. Free; all venereal diseases.

Morgan, Calhoun Co.: Morgan Clinic. Free; all venereal diseases.

Morven, Brooks Co.: Morven Clinic. Free; syphilis only.

Moultrie, Colquitt Co.: Moultrie Clinic, 15 First Ave. NW. Free; syphilis only.

Nahunta, Brantley Co.: Brantley Co. Health Center. Free; syphilis only.

Newman, Coweta Co.: Newman V. D. Clinic, County Welfare Building. Free; syphilis only.

Norman Park, Colquitt Co.: Norman Park Clinic. Free; syphilis only.

Ochlochnee, Thomas Co.: Ochlochnee Prenatal Clinic. Free; all venereal diseases.

Omega, Tift Co.: Omega Clinic. Free; syphilis only.

Palmetto, Fulton Co.: Palmetto Health Center. Free; syphilis only.

Parrott, Terrell Co.: Parrott Clinic, Terrell Co. Health Department. Free; syphilis only.
Pavo, Brooks Co.: Pavo Clinic. Free; syphilis only.
Pearson, Atkinson Co.: Pearson V. D. Clinic. Free; all venereal diseases.
Pelham, Mitchell Co.: W. M. S. Clinic. Part-pay; syphilis only.
Piscola, Brooks Co.: Piscola Clinic. Free; syphilis only.
Portal, Bulloch Co.: Portal Clinic. Free; syphilis only.
Quitman, Brooks Co.: Quitman Clinic. Free; syphilis only.
Register, Bulloch Co.: Register Clinic, Route 1. Free; syphilis only.
Reynolds, Taylor Co.: Venereal Disease Clinic. Free; syphilis only.
Reynoldsville, Seminole Co.: Reynoldsville Clinic. Free; syphilis and gonorrhea only.
Riceboro, Liberty Co.: Riceboro Clinic. Free; syphilis only.
Ringgold, Catoosa Co.: Ringgold Venereal Disease Clinic, Health Department. Free; syphilis only.
Rome, Floyd Co.:
Mull-Moss Clinic. Part-pay; all venereal diseases.
Rome Clinic. Free; syphilis only.
Samaritan Clinic. Free; syphilis only.
Rossville, Walker Co.: Rossville V. D. Clinic, Walker Co. Health Department. (White only.) Free; syphilis only.
Roswell, Fulton Co.: Roswell Health Center. Free; syphilis only.
Royston, Franklin Co.: Royston Clinic. Free; syphilis and gonorrhea only.
St. George, Charlton Co.: St. George Clinic. (Negro only.) Free; syphilis only.
St. Marys, Camden Co.: St. Marys Clinic, Mobile Unit, Old Courthouse. Free; all venereal diseases.
Sandersville, Washington Co.: Prenatal Clinic. (Female only.) Free; syphilis only.
Sardis, Burke Co.: Sardis Clinic. Free; syphilis only.
Sasser, Terrell Co.: Sasser Clinic, Terrell Co. Health Department. Free; syphilis only.
Savannah, Chatham Co.: Savannah Clinic. Free; all venereal diseases.
Screven, Wayne Co.: Screven Clinic. Free; syphilis only.
Shady Dale, Jasper Co.: Shady Dale Clinic. Free; all venereal diseases.
Smithville, Lee Co.: Venereal Disease Clinic, Lee Co. Health Department. Free; syphilis only.
Sparta, Hancock Co.: Child Health Demonstration Clinic. Free; all venereal diseases.
Springfield, Effingham Co.: Springfield Clinic. Free; syphilis only.
Statesboro, Bulloch Co.: Statesboro Clinic. Free; syphilis only.
Sterling, Glynn Co.: Sterling Clinic, Mobile Unit, Schoolhouse. Free; all venereal diseases.
Stockton, Lanier Co.: Stockton Clinic. Free; all venereal diseases.
Stone Mountain, De Kalb Co.: De Kalb Co. Board of Health, Office of Dr. Willis T. McCurdy. Free; all venereal diseases.
Sylvania, Screven Co.: Venereal Disease Clinic. Part-pay; syphilis only.
Sylvester, Worth Co.: Sylvester Clinic. Free; all venereal diseases.
Thomaston, Upson Co.: Upson Clinic, Courthouse. Free; syphilis only.
Thomasville, Thomas Co.: Health Department. Free; all venereal diseases.
Tifton, Tift Co.: Tifton Clinic. Free; syphilis only.
Toccoa, Stephens Co.: Stephens Co. Clinic. Free; all venereal diseases.

Townsend, McIntosh Co.:
Ardock Clinic, Mobile Unit, General Store. Free; all venereal diseases.
Cannon Bluff Clinic, Mobile Unit, Schoolhouse. Free; all venereal diseases.
Harris Neck Clinic, Mobile Unit, General Store. Free; all venereal diseases.
Jones Clinic, Mobile Unit, Schoolhouse. Free; all venereal diseases.
Shellman Bluff Clinic, Mobile Unit, Schoolhouse. Free; all venereal diseases.
Townsend Clinic, Mobile Unit, Railway Station. Free; all venereal diseases.
Warsaw Clinic, Mobile Unit, General Store. Free; all venereal diseases.

Ty Ty, Tift Co.: Ty Ty Clinic. Free; syphilis only.

Union Point, Green Co.: Union Point Clinic. Free; syphilis only.

Valdosta, Lowndes Co.: Lowndes Co. Board of Health. Free; all venereal diseases.

Vidalia, Toombs Co.: Vidalia Clinic. Free; all venereal diseases.

Vidette, Burke Co.: Vidette Clinic. Free; syphilis only.

Warm Springs, Meriwether Co.: Warm Springs Foundation Clinic. Free; syphilis only.

Waverly, Camden Co.:
Spring Bluff, Mobile Unit, Turpentine Still. Free; all venereal diseases.
Waverly Clinic, Mobile Unit, Post Office. Free; all venereal diseases.

Waverly Hall, Harris Co.: Waverly Hall Clinic. Free; syphilis only.

Waycross, Ware Co.: Ware Co. V. D. Clinic. Part-pay; syphilis only.

Waynesboro, Burke Co.: Waynesboro Clinic, Courthouse. Free and pay; syphilis only.

Ways Station, Bryan Co.: Venereal Disease Clinic. Free; all venereal diseases.

West Point, Troup Co.: West Point Clinic. Free; syphilis only.

Whigham, Grady Co.: City Hall Clinic. Free; all venereal diseases.

White Oak, Camden Co.: Tarboro Clinic, Mobile Unit, General Store. Free; all venereal diseases.

Willacoochee, Atkinson Co.: Willacoochee V. D. Clinic. Free; all venereal diseases.

Woodbine, Camden Co.:
Colesburg Clinic, Mobile Unit, Filling Station. Free; all venereal diseases.
Woodbine Clinic. Free; all venereal diseases.
Woodbine Clinic, Mobile Unit, Courthouse. Free; all venereal diseases.

Wrens, Jefferson Co.: Wrens Clinic. Free; all venereal diseases.

IDAHO

Boise, Ada Co.: Ada Co. Health Unit, 618 Eastman Bldg. Free; syphilis and gonorrhea.

Coeur d'Alene, Kootenai Co.: Kootenai Co. Health Unit. Free; syphilis and gonorrhea.

Idaho Falls, Bonneville Co.: Bonneville Co. Health Unit, Rogers Bldg. Free; syphilis and gonorrhea.

Lewiston, Nez Perce Co.: North Central District Health Unit. Free; syphilis and gonorrhea.

Pocatello, Bannock Co.: Bannock Co. Health Unit, 825 West Center St. Free; syphilis and gonorrhea.

Twin Falls, Twin Falls Co.: South Central District Health Unit. Free; syphilis and gonorrhea.

Wallace, Shoshone Co.: Shoshone Co. Health Unit. Free; syphilis and gonorrhea.

ILLINOIS

Alton, Madison Co.: Alton V. D. Clinic, 101 East Third St. Free; all venereal diseases.

Aurora, Kane Co.: Aurora Venereal Disease Clinic, 52 Downer Place. Free; all venereal diseases.

Berwyn, Cook Co.: Berwyn Social Hygiene Clinic, 6600 West 26th St. Free; all venereal diseases.

Bloomington, McLean Co.: McLean Co. Venereal Disease Treatment Center, 404 American State Bank Bldg. Free; all venereal diseases.

Cairo, Alexander Co.: Social Hygiene Clinic, 1101 Cedar St. Free; all venereal diseases.

Calumet City, Cook Co.: Free Treatment Center, City Hall. Free; all venereal diseases.

Champaign, Champaign Co.: Champaign-Urbana Public Health District, 307 South Wright St. Free; all venereal diseases.

Chicago, Cook Co.:

Billings Hospital Clinics, The University of Chicago, 950 East 59th St. (White only.) Pay; all venereal diseases.

The Central Free Dispensary of West Chicago, Inc., 1748 West Harrison St. Free and part-pay; all venereal diseases.

Chicago Medical School Clinic, 710 South Wolcott Ave. Free and part-pay; all venereal diseases.

Chicago State Hospital, 6400 Irving Park. Free; all venereal diseases.

The Children's Memorial Hospital, 707 Fullerton Ave. (Children only.) Free; syphilis only.

Cook Co. Children's Hospital, 1850 West Harrison St. (Children only.) Free; all venereal diseases.

Cook Co. Hospital, Obstetrics, 1850 West Harrison St. (Female adults only) Free; syphilis only.

Cook Co. Hospital, Neurology, 1850 West Harrison St. (Adults only.) Free; syphilis only.

Cook Co. Hospital, Dermatology, 1800 West Harrison St. (Adults only.) Free; syphilis only.

Cook Co. Jail Social Hygiene Clinic, 2600 South California Ave. Free; all venereal diseases.

Ehrlich Clinic, 1362 South Halsted St. Free; syphilis and gonorrhea only.

Frances Juvenile Home Association, 5141 South Michigan Ave. (White children only.) Part-pay; all venereal diseases.

Grant Hospital, 551 Grant Place. (White only.) Free and pay or part-pay; syphilis only.

House of Correction Social Hygiene Clinic, 26th and California Ave. Free; all venereal diseases.

Illinois Charity Eye and Ear Infirmary, 904 W. Adams St. Free; syphilis only.

Illinois Research, 1819 West Polk St. Free; all venereal diseases.

Illinois Social Hygiene League, 9 East Huron St. Free and pay or part-pay; all venereal diseases.

Mandel Clinic, Michael Reese Hospital, 29th St. and Ellis Ave. Free and part-pay; all venereal diseases.

Mercy Free Dispensary, 2526 Calumet Ave. Free and pay or part-pay; all venereal diseases.

Chicago, Cook Co.—Continued.

Montgomery Ward Clinic, 747 Fairbanks Court. Free and pay or part-pay; all venereal diseases.

Mt. Sinai Dispensary, 1519 South California Ave. (White only.) Free and pay or part-pay; all venereal diseases.

Municipal Children's Gonorrhea Clinic, 27 East 26th St. (Children only.) Free; gonorrhea only.

Municipal Children's Syphilis Clinic, 27 East 26th St. (Children only.) Free; syphilis only.

Municipal Children's Syphilis Clinic, 4253 South State St. (Children only.) Free; syphilis only.

Municipal Premarital Examination Clinic, 54 West Hubbard St. Free; all venereal diseases.

Municipal Prenatal Social Hygiene Clinic, 27 East 26th St. (Female only.) Free; all venereal diseases.

Municipal Prenatal Social Hygiene Clinic, 4253 South State St. (Female only.) Free; all venereal diseases.

Municipal Social Hygiene Clinic, 27 East 26th St. Free; all venereal diseases.

Municipal Tuberculosis Sanitarium, 5601 North Crawford Ave. Free; all venereal diseases.

Municipal Venereal Disease Diagnostic Clinic, Municipal Courts Bldg., 1121 South State St. Free; all venereal diseases.

Parkway Lodge, 5120 South Parkway. Free; all venereal diseases.

Post Graduate Hospital and Medical School, 2400 South Dearborn St. Part-pay; all venereal diseases.

Provident Hospital, 426 East 51st St. Part-pay; all venereal diseases.

Public Health Institute (Loop), 159 North Dearborn St. Part-pay; all venereal diseases.

Public Health Institute (South Side), 129 East 31st St. Part-pay; all venereal diseases.

Salvation Army Maternity Hospital, 5040 North Pulaski Road. (Female only.) Free; syphilis only.

St. Luke's Hospital Clinic, 1439 South Michigan Ave. Part-pay; all venereal diseases.

Stockyards Clinic, University of Chicago-Billings Hospital, 734 West 47th St. (Adults only.) Free; syphilis only.

Women and Children's Hospital, 1600 Maypole Ave. Free and pay or part-pay; all venereal diseases.

Chicago Heights, Cook Co.: Chicago Heights Clinic, St. James Hospital. Free; all venereal diseases.

Cicero, Cook Co.: Cicero Clinic, 5341 West Cermak Road. Free; all venereal diseases.

Decatur, Macon Co.: Decatur and Macon Co. Hospital Clinic, 2300 North Edwards St. Free; all venereal diseases.

East St. Louis, St. Clair Co.: Social Hygiene Clinic, 325 East Broadway. Free; all venereal diseases.

Evanston, Cook Co.: Evanston Venereal Disease Clinic, 1806 Maple Ave. Free; all venereal diseases.

Granite City, Madison Co.: Social Hygiene Clinic, St. Elizabeth's Hospital. Free; all venereal diseases.

Harvey, Cook Co.: Harvey Clinic, City Hall. Free; all venereal diseases.

Herrin, Williamson Co.: Free Treatment Center, 110 West Cherry St. Free; all venereal diseases.

Jacksonville, Morgan Co.: Morgan County Clinic, Passavant Hospital. Free; all venereal diseases.

La Salle, La Salle Co.: Hygiene Institute, 151 Fifth St. Free; all venereal diseases.

Madison, Madison Co.: Madison V. D. Clinic, 411 Second St. Free; all venereal diseases.

Maywood, Cook Co.: Social Hygiene Clinic, Maywood Health Center, 103 South 5th Ave. Free; all venereal diseases.

Metropolis, Massac Co.: Dr. J. A. Fisher's Clinic, 205 Metropolis St. Free; all venereal diseases.

Moline, Rock Island Co.: Social Hygiene Clinic, 1530 Second Ave. Free; all venereal diseases.

New Shawneetown, Gallatin Co.: New Shawneetown Clinic. Free; all venereal diseases.

Peoria, Peoria Co.:

Venereal Disease Clinic of the Department of Health, 508 Main St. Free; all venereal diseases.

Venereal Disease Clinic of the Department of Health, 203 City Hall. Free; all venereal diseases.

Quincy, Adams Co.: Quincy Venereal Clinic, 206 Majestic Bldg. Free; all venereal diseases.

Robbins, Cook Co.: Robbins Clinic, Blue Island-Robbins Venereal Disease Treatment Center, 3421 West 137th St. Free; all venereal diseases.

Rockford, Winnebago Co.: City Health Center, 402 Mead Building. Free; all venereal diseases.

Sparta, Randolph Co.: Free Treatment Center, 209 West Jackson St. Free; all venereal diseases.

Waukegan, Lake Co.: Lake Co. Free Treatment Center, 67 Washington St. Free; all venereal diseases.

INDIANA

Anderson, Madison Co.: Public Health Venereal Clinic, City Hall. Free; all venereal diseases.

Bicknell, Knox Co.: Public Health Venereal Clinic, City Hall. Free; all venereal diseases.

Bloomington, Monroe Co.: Public Health Clinic, City Hall. Free; syphilis and gonorrhea.

Boonville, Warrick Co.: Public Health Venereal Clinic, Courthouse. Free; all venereal diseases.

Brazil, Clay Co.: Public Health Venereal Clinic, Clay Co. Hospital. Free and pay or part-pay; syphilis only.

Columbus, Bartholomew Co.: Public Health Venereal Clinic, Courthouse. Free; all venereal diseases.

East Chicago, Lake Co.: Public Health Venereal Clinic, City Hall. Free; all venereal diseases.

Evansville, Vanderburgh Co.: Public Health Venereal Clinic, Courthouse Annex. Free; all venereal diseases.

Fort Wayne, Allen Co.: Public Health Venereal Clinic, City Hall, Third Floor. Free and part-pay; all venereal diseases.

Gary, Lake Co.: Gary Health Center, City Hall. Free; all venereal diseases.

Hammond, Lake Co.: Public Health Venereal Clinic, City Hall. Free; all venereal diseases.

Indianapolis, Marion Co.:

Indiana University Medical Center, Coleman Hospital Clinic for Women, 1040–1232 West Michigan St. (White women only.) Free; all venereal diseases.

Indianapolis City Hospital, Dermatology and Syphilology Clinic, 960 Locke St. Free; all venereal diseases.

Indianapolis City Hospital, Vulvovaginitis Clinic. Free.

Riley Clinic for Children, 1040–1232 West Michigan St. (Children only.) Free; all venereal diseases.

Robert W. Long Hospital for Adults, 1040–1232 West Michigan St. (White adults only.) Free; all venereal diseases.

Venereal Diseases Clinic, 960 Locke St. (Adults only.) Part-pay; all venereal diseases.

Kokomo, Howard Co.: Public Health Venereal Clinic, 107½ S. Union St. Free; all venereal diseases.

Madison, Jefferson Co.: Public Health Venereal Clinic, No. 2 Engine House. Free; all venereal diseases.

Marion, Grant Co.: Marion Social Hygiene Clinic, City Hall. Free; syphilis only.

Muncie, Delaware Co.: Public Health Venereal Clinic, Room 10, Anthony Block Bldg. Free; all venereal diseases.

New Albany, Floyd Co.: Public Health Venereal Clinic, 217 East Spring St. Free; syphilis only.

Princeton, Gibson Co.: Public Health Venereal Clinic, 115 North Prince St. Free; all venereal diseases.

Richmond, Wayne Co.: Public Health Venereal Clinic, 26 South 7th St. Free; all venereal diseases.

Shelbyville, Shelby Co.: Public Health Venereal Clinic, 20 N. Pike St. Free; syphilis only.

South Bend, St. Joseph Co.: Public Health Venereal Clinic, 114½ South Lafayette Blvd. Free; all venereal diseases.

Terre Haute, Vigo Co.: Public Health Venereal Clinic, City Hall. Part-pay; all venereal diseases.

Wabash, Wabash Co.: Public Health Venereal Clinic, Wabash Co. Hospital. Free; syphilis only.

IOWA

Burlington, Des Moines Co.: Des Moines Co. Clinic, City Hall. Free; all venereal diseases.

Cedar Rapids, Linn Co.: Linn Co. Clinic, Room 11, Courthouse. Part-pay; all venereal diseases.

Clinton, Clinton Co.: Clinton Co. Clinic, 601 Wilson Bldg. Free; all venereal diseases.

Davenport, Scott Co.: Scott Co. Health Center, 523 Main St. Free; all venereal diseases.

Des Moines, Polk Co.: Broadlawns General Hospital, 406 Center St. Free; all venereal diseases.

Dubuque, Dubuque Co.: Dubuque Co. Clinic, City Hall, 13th and Central Ave. Free; all venereal diseases.

Fort Dodge, Webster Co.: Webster Co. Clinic, Cor. First Ave. South and 8th St. Free; all venereal diseases.

Keokuk, Lee Co.: Lee Co. Clinic, 601–03 Main St. Free; all venereal diseases.
Muscatine, Muscatine Co.: Muscatine Co. Clinic, 111 Cedar St. Free; all venereal diseases.
Oskaloosa, Mahaska Co.: Mahaska Co. Clinic, 107½ High Ave., East. Free; all venereal diseases.
Ottumwa, Wapello Co.: Wapello Co. Clinic, Courthouse. Free; all venereal diseases.
Sioux City, Woodbury Co.: Woodbury Co. Medical Clinic, 315 Sixth St. Free; all venereal diseases.
Washington, Washington Co.: Washington Co. Health Unit. Free; syphilis only.
Waterloo, Black Hawk Co.: Black Hawk Co. Clinic, Tribune Press Bldg. Free; all venereal diseases.

KANSAS

Columbus, Cherokee Co.: Cherokee Co. Clinic. Free; all venereal diseases.
Emporia, Lyon Co.: Lyon Co. Clinic, Office of Dr. H. C. Nutting, 527 Commercial St. Free; all venereal diseases.
Hutchinson, Reno Co.: Reno Co. Clinic, Courthouse. Free; all venereal diseases.
Junction City, Geary Co.: Geary Co. Venereal Disease Clinic, Office of Dr. C. V. Minnick. Free; all venereal diseases.
Kansas City, Wyandotte Co.:
City Hall Clinic, 6th and Ann Ave. Free; all venereal diseases.
University of Kansas Hospital, 39th and Rainbow Sts. Free and pay or part-pay; all venereal diseases.
Lansing, Leavenworth Co.:
Kansas State Penitentiary. (Male, adults, only.) Free; all venereal diseases.
Women's Quarantine Hospital, Kansas State Industrial Farm. (Female, adults, only.) Free; all venereal diseases.
Lawrence, Douglas Co.: Douglas Co. Clinic, City Hall. Free; all venereal diseases.
Leavenworth, Leavenworth Co.: Leavenworth Co. Clinic, Broadway and Reese St. Free; all venereal diseases.
Parsons, Labette Co.: Labette Co. Public Health Clinic, 112½ South 18th St. Free; all venereal diseases.
Salina, Salina Co.: Salina Co. Clinic, 617 United Life Bldg. Free; all venereal diseases.
Topeka, Shawnee Co.: City Clinic, City Hall. Free and part-pay; all venereal diseases.
Wichita, Sedgwick Co.: Sedgwick Co. Clinic, 300 South Broadway. Free; all venereal diseases.

KENTUCKY

Adairville, Logan Co.: Logan Co. Clinic, Square. Free; all venereal diseases.
Albany, Clinton Co.: Clinton Co. Health Department. Free and part-pay; all venereal diseases.
Anchorage, Jefferson Co.: Griffytown Clinic. Free; all venereal diseases.
Ashland, Boyd Co.: Boyd Co. Health Department Office. Free: all venereal diseases.

Kentucky

Barbourville, Knox Co.: Knox Co. Health Department Office. Free; all venereal diseases.

Bardwell, Carlisle Co.: Carlisle Co. Health Department Office. Free and pay or part-pay; all venereal diseases.

Bedford, Trimble Co.: Trimble Co. Health Department Office. Free and part-pay; all venereal diseases.

Benton, Marshall Co.: Marshall Co. Health Department Office. Free and part-pay; all venereal diseases.

Berea, Madison Co.: Madison Co. Health Department Office. Free and part-pay; all venereal diseases.

Birmingham, Marshall Co.: Rock Quarry Clinic. (T. V. A. employees.) Free; syphilis only.

Bowling Green, Warren Co.: Warren Co. Health Department Office, City Hall. Free and part-pay; all venereal diseases.

Brownsville, Edmonson Co.: Edmonson Co. Health Department Office. Free; all venereal diseases.

Burkesville, Cumberland Co.: Cumberland Co. Health Department Office. Free and part-pay; all venereal diseases.

Cadiz, Trigg Co.: Trigg Co. Health Department Office. Free; all venereal diseases.

Camp Taylor, Jefferson Co.: Camp Taylor Clinic, 1430 Lincoln St. (White only.) Free; all venereal diseases.

Campton, Wolfe Co.: Wolfe Co. Health Department Office. Part-pay; all venereal diseases.

Carlisle, Nicholas Co.: Nicholas Co. Health Department Office. Free; all venereal diseases.

Carrollton, Carroll Co.: Carroll Co. Health Department Office. Free; all venereal diseases.

Central City, Muhlenberg Co.: Muhlenberg Co. Clinic, City Bldg. Free and part-pay; all venereal diseases.

Clinton, Hickman Co.: Hickman Co. Health Department Office, Clinton Bank Bldg. Free and part-pay; all venereal diseases.

Columbia, Adair Co.: Adair Co. Health Department Office. Free; all venereal diseases.

Corbin, Whitley Co.: Whitley Co. Health Department Office. Free; all venereal diseases.

Covington, Kenton Co.: Kenton Co. Health Department Office, 912 Scott St. Free and part-pay; all venereal diseases.

Dixon, Webster Co.: Webster Co. Health Department Office. Free; all venereal diseases.

Eddyville, Lyon Co.: Lyon Co. Health Department Office. Free and part-pay; all venereal diseases.

Edmonton, Metcalfe Co.: Metcalfe Co. Health Department Office. Free; all venereal diseases.

Elizabethtown, Hardin Co.: Hardin Co. Health Department, Long Bldg. Free and part-pay; all venereal diseases.

Elkton, Todd Co.: Todd Co. Health Department Office. Free; all venereal diseases.

Flemingsburg, Fleming Co.: Fleming Co. Health Department Office. Free and part-pay; all venereal diseases.

Fredonia, Caldwell Co.: Caldwell Co. Health Department Office. Free; all venereal diseases.

Frenchburg, Menifee Co.: Menifee Co. Health Department Office. Free; all venereal diseases.

Fullerton, Greenup Co.: Greenup Co. Health Department Office. Free; all venereal diseases.

Fulton, Fulton Co.: Fulton Co. Health Department Office. Free and part-pay; all venereal diseases.

Georgetown, Scott Co.: Scott Co. Health Department Office. Free and part-pay; all venereal diseases.

Gilbertsville, Marshall Co.: T. V. A. Hospital. (Employees only.) All venereal diseases.

Glasgow, Barren Co.: Barren Co. Health Department Office. Free and part-pay; all venereal diseases.

Grayson, Carter Co.: Carter Co. Health Department Office. Free; all venereal diseases.

Greensburg, Green Co.: Green Co. Health Department Office. Free; all venereal diseases.

Greenup, Greenup Co.: Greenup Co. Health Department Office. Free; all venereal diseases.

Greenville, Muhlenberg Co.: Muhlenberg Co. Health Department Office, Bailey Bldg. Free and part-pay; all venereal diseases.

Harrodsburg, Mercer Co.: Mercer Co. Health Department Office. Free; all venereal diseases.

Hartford, Ohio Co.: Ohio Co. Health Department Office. Free; all venereal diseases.

Hawesville, Hancock Co.: Hancock Co. Health Department Office. Free and part-pay; all venereal diseases.

Hazard, Perry Co.: Perry Co. Health Department Office. Free and part-pay; all venereal diseases.

Henderson, Henderson Co.: Henderson Co. Health Department Office, City Bldg. Free; all venereal diseases.

Hickman, Fulton Co.: Fulton Co. Health Department Office. (White only.) Free; all venereal diseases.

Hindman, Knott Co.: Knott Co. Health Department Office. Free and part-pay; all venereal diseases.

Hodgenville, La Rue Co.: La Rue Co. Health Department Office. Free and part-pay; all venereal diseases.

Horse Cave, Hart Co.: Hart Co. Health Department Office. Free; all venereal diseases.

Hyden, Leslie Co.: Leslie Co. Health Department Office. Free; all venereal diseases.

Inez, Martin Co.: Martin Co. Health Department Office. Free and part-pay; all venereal diseases.

Irvine, Estill Co.: Estill Co. Health Department Office. Free and part-pay; all venereal diseases.

Jackson, Breathitt Co.: Breathitt Co. Health Department Office. Free and part-pay; all venereal diseases.

La Center, Ballard Co.: Ballard Co. Health Department Office. Free; all venereal diseases.

Lawrenceburg, Anderson Co.: Anderson Co. Health Department Office, Main St. Free; all venereal diseases.

Lexington, Fayette Co.: Fayette Co. Health Department Office, 212 N. Upper St. Free; all venereal diseases.

Lewisport, Hancock Co.: Hancock Co. Health Department Office. Part-pay; all venereal diseases.

Liberty, Casey Co.: Casey Co. Health Department Office. Free; all venereal diseases.

London, Laurel Co.: Laurel Co. Health Department Office, Main St. Free and part-pay; all venereal diseases.

Louisa, Lawrence Co.: Lawrence Co. Health Department Office. Free; all venereal diseases.

Louisville, Jefferson Co.:

Central Clinic, 920 West Chestnut St. (Negro only.) Free and part-pay; syphilis only.

City Hospital, Preston and Chestnut St. Free and part-pay; all venereal diseases.

East Clinic, 1076 Washington St. Free and part-pay; syphilis only.

Highland Park Clinic, Crittenden Drive and Hiawatha St. Free and part-pay; syphilis only.

Jefferson Co. Health Department Office, Fiscal Court Bldg. Free; all venereal diseases.

Jefferson Co. Jail Clinic. (Adults only.) Free; all venereal diseases.

Jefferson Co. Workhouse, 1388 Payne St. (Adults only.) Free; all venereal diseases.

Newburg Clinic, Route 1. (Negro only.) Free; all venereal diseases.

Portland Clinic, 2318 Portland St. Free and part-pay; syphilis only.

McKee, Jackson Co.: Jackson Co. Health Department Office. Free; all venereal diseases.

Madisonville, Hopkins Co.: Hopkins Co. Health Department Office, Courthouse. Free; all venereal diseases.

Manchester, Clay Co.: Clay Co. Health Department Office. Free; all venereal diseases.

Marion, Crittenden Co.: Crittenden Co. Health Department Office. Free; all venereal diseases.

Mayfield, Graves Co.: Graves Co. Health Department Office. Free; all venereal diseases.

Maysville, Mason Co.: Mason Co. Health Department Office. Free and part-pay; all venereal diseases.

Middlesboro, Bell Co.: Bell Co. Health Department Office. Free; all venereal diseases.

Morehead, Rowan Co.: Rowan Co. Health Department Office. Free; all venereal diseases.

Morganfield, Union Co.: Union Co. Health Department Office, Courthouse. Free and part-pay; all venereal diseases.

Morgantown, Butler Co.: Butler Co. Health Department Office. Free and part-pay; all venereal diseases.

Mt. Vernon, Rockcastle Co.: Rockcastle Co. Health Department Office. (White only.) Free; all venereal diseases.

Muldraugh, Meade Co.: Meade Co. Health Department Office. Free and part-pay; all venereal diseases.

Munfordville, Hart Co.: Hart Co. Health Department Office. Free; all venereal diseases.

Murray, Calloway Co.: Calloway Co. Health Department Office. (Adults only.) Free; all venereal diseases.

Newport, Campbell Co.: Campbell Co. Clinic, Fourth and York Sts. Free and part-pay; all venereal diseases.

Owenton, Owen Co.: Owen Co. Health Department Office. Free; all venereal diseases.

Owingsville, Bath Co.: Bath Co. Health Department Office. Free; all venereal diseases.

Paducah, McCracken Co.: McCracken Co. Health Department Office, 524 North 4th St. Free and part-pay; all venereal diseases.

Paintsville, Johnson Co.: Johnson Co. Health Department Office, Court St. (White only.) Free; all venereal diseases.

Pikesville, Pike Co.: Pike Co. Health Department Office. Free and part-pay; all venereal diseases.

Pineville, Bell Co.: Bell Co. Health Department Office. Free; all venereal diseases.

Prestonsburg, Floyd Co.: Floyd Co. Health Department Office, Court St. Free; all venereal diseases.

Princeton, Caldwell Co.: Caldwell Co. Health Department Office, East Main St. Free; all venereal diseases.

Richmond, Madison Co.: Madison Co. Health Department Office, Federal Bldg. Free and part-pay; all venereal diseases.

Russell, Greenup Co.: Greenup Co. Health Department Office. Free; all venereal diseases.

Russellville, Logan Co.: Logan Co. Health Department Office, North Main St. Free; all venereal diseases.

Salem, Livingston Co.: Livingston Co. Health Department Office. Free and part-pay; all venereal diseases.

Sass Ridge, Fulton Co.: Fulton Co. Health Department Office. Free; all venereal diseases.

Scottsville, Allen Co.: Allen Co. Health Department Office. Free; all venereal diseases.

Smithland, Livingston Co.: Livingston Co. Health Department Office. Free and part-pay; all venereal diseases.

Somerset, Pulaski Co.: Pulaski Co. Health Department Office. Free; all venereal diseses.

Stanford, Lincoln Co.: Lincoln Co. Health Department Office. Free; all venereal diseases.

Stanton, Powell Co.: Powell Co. Health Department Office. Free; all venereal diseases.

Taylorsville, Spencer Co.: Spencer Co. Health Department Office, Main St. Free; all venereal diseases.

Warsaw, Gallatin Co.: Gallatin Co. Health Department Office. Free; all venereal diseases.

West Liberty, Morgan Co.: Morgan Co. Health Department Office. Free; all venereal diseases.

Whitesburg, Letcher Co.: Letcher Co. Health Department Clinic. Free; all venereal diseases.

Whitley City, McCreary Co.: McCreary Co. Health Department Office. Free; all venereal diseases.

Wickliffe, Ballard Co.: Ballard Co. Health Department Office. Free; all venereal diseases.

Williamsburg, Whitley Co.: Whitley Co. Health Department Office, Courthouse. Free; all venereal diseases.

Williamstown, Grant Co.: Grant Co. Health Department Office. Free; all venereal diseases.

Yeaddiss, Leslie Co.: Leslie Co. Health Department Office. Free; all venereal diseases.

LOUISIANA

Abbeville, Vermillion Parish: Vermillion Parish Health Unit. Free; syphilis only.

Alexandria, Rapides Parish: Rapides Parish Health Unit, Charity Hospital. Free; syphilis only.

Arcadia, Bienville Parish: Bienville Parish Health Unit. Free; syphilis only.

Athens, Claiborne Parish: Claiborne Parish Health Unit. Free; syphilis only.

Bastrop, Morehouse Parish: Morehouse Parish Health Unit. Free; syphilis only.

Batchelor, Pointe Coupee Parish: Point Coupee Parish Health Unit. Free; syphilis only.

Bernice, Union Parish: Union Parish Health Unit. Free; syphilis only.

Brownview, Pointe Coupee Parish: Pointe Coupee Parish Health Unit. Free; syphilis only.

Caspiana, Caddo Parish: Caddo Parish Health Unit. Free; syphilis only.

Church Point, Acadia Parish: Acadia Clinic. Free; syphilis only.

Colfax, Grant Parish: Grant Parish Health Unit. Free; syphilis only.

Coushatta, Red River Parish: Red River Parish Health Unit. Free; syphilis only.

Covington, St. Tammany Parish: St. Tammany Parish Health Unit. Free; all venereal diseases.

Crowley, Acadia Parish:

Acadia Parish Health Unit. Free; syphilis only.

Rayne Clinic. Acadia Parish Health Unit. Free; syphilis only.

Destrehan, St. Charles Parish: St. Charles Parish Clinic. Free: syphilis only.

Dixie, Caddo Parish: Caddo-Shreveport Health Unit. Free; syphilis only.

Evening Star, Caddo Parish: Caddo-Shreveport Health Unit. Free; syphilis only.

Farmerville, Union Parish: Union Parish Health Unit. Free; syphilis only.

Franklin, St. Mary Parish: St. Mary Parish Health Unit, Health Center. Free; syphilis only.

Franklinton, Washington Parish: Washington Parish Health Unit. Free; syphilis only.

Gilliam, Caddo Parish: Caddo-Shreveport Health Unit. Free; syphilis only.

Good Pine, LaSalle Parish: LaSalle Parish Health Unit. Free; syphilis only.

Gueydan, Vermillion Parish: Vermillion Parish Health Unit. Free; syphilis only.

Haynesville, Claiborne Parish: Claiborne Parish Health Unit. Free; syphilis only.

Homer, Claiborne Parish: Claiborne Parish Health Unit. Free; syphilis only.

Houma, Terrebonne Parish: Terrebonne Parish Health Unit, 1029 East Main St. Free; syphilis only.

Jeanerette, Iberia Parish: Iberia Parish Health Unit. Free; syphilis only.

Jena, LaSalle Parish: LaSalle Parish Health Unit. Free; syphilis only.

Jennings, Jefferson Davis Parish: Jefferson Davis Parish Health Unit, Courthouse. Free; syphilis only.

Lafayette, Lafayette Parish: Lafayette Charity Hospital, St. Mary. Free; syphilis only.

Lake Arthur, Jefferson Davis Parish: Jefferson Davis Parish Health Unit, Holloway Bldg. Free; syphilis only.

Lake Providence, East Carroll Parish: East Carroll Parish Health Unit. Free; syphilis only.

Liberty, Caddo Parish: Caddo Parish Health Unit. Free; syphilis only.

Lisbon, Claiborne Parish: Claiborne Parish Health Unit. Free; syphilis only.

Logansport, DeSoto Parish: DeSoto Parish Health Unit. Free; syphilis only.

Luling, St. Charles Parish: St. Charles Parish Health Unit. Free; syphilis only.

Mamou, Evangeline Parish: Evangeline Parish Health Unit. Free; syphilis only.

Mansfield, DeSoto Parish: DeSoto Parish Health Unit. Free; syphilis only.

Maringouin, Iberville Parish: Iberville Parish Health Unit. Free; syphilis only.

Minden, Webster Parish: Webster Parish Health Unit. Free; syphilis only.

Mira, Caddo Parish: Caddo Parish Health Unit. Free; syphilis only.

Monroe, Ouachita Parish: Ouachita Parish Health Unit. Free; all venereal diseases.

Morgan City, St. Mary Parish: St. Mary Parish Health Unit. Free; syphilis only.

Mount Olive, Caddo Parish: Caddo Parish Health Unit. Free; all venereal diseases.

Natchitoches, Natchitoches Parish: Natchitoches Parish Health Unit. Free; syphilis only.

Newellton, Tensas Parish: Tensas Parish Health Unit. Free; syphilis only.

New Iberia, Iberia Parish: Iberia Parish Health Unit. Free; syphilis only.

New Orleans, Orleans Parish:

Charity Hospital, 1532 Tulane Ave. Free; all venereal diseases.

Flint Goodridge Clinic, 2425 Louisiana Ave. (Negro only.) Part-pay; all venereal diseases.

Hutchinson Memorial Hospital, Tulane Ave. Free; all venereal diseases.

Touro Infirmary, 3516 Prytania St. Free and part-pay; all venereal diseases.

New Roads, Pointe Coupee Parish: Pointe Coupee Parish Health Unit. Free; syphilis only.

Oakdale, Allen Parish: Allen Parish Health Unit, South Tenth St. Free; syphilis only.

Oak Grove, West Carroll Parish: West Carroll Parish Health Unit. Free; syphilis only.

Oak Ridge, Morehouse Parish: Morehouse Parish Health Unit. Free; syphilis only.

Oberlin, Allen Parish: Allen Parish Health Unit. Free; syphilis only.

Plaquemine, Iberville Parish: Iberville Parish Health Unit, House Clinic, Plaquemine Court. Free; syphilis only.

Robson, Caddo Parish: Caddo-Shreveport Health Unit. Free; syphilis only.

Ruston, Lincoln Parish: Lincoln Parish Health Unit. Free; syphilis only.

St. Joseph, Tensas Parish: Tensas Parish Health Unit. St. Joseph Clinic. Free; syphilis only.

St. Martinville, St. Martin Parish: St. Martin Parish Health Unit, 201–202 Courthouse Bldg. Free; syphilis and gonorrhea only.

Shreveport, Caddo Parish:

Caddo-Shreveport Health Unit, Municipal Auditorium. Milam and Grand Sts. Free; syphilis only.

Caddo-Shreveport Health Unit, Parish Farm. Free; syphilis only.

Spring Hill, Webster Parish: Webster Parish Health Unit. Free; syphilis only.

Thibodaux, La Fourche Parish: La Fourche Parish Health Unit. Free; syphilis only.

Ville Platte, Evangeline Parish: Evangeline Parish Health Unit. Free; syphilis only.

Vivian, Caddo Parish: Caddo-Shreveport Health Unit. Free; syphilis only.

Waterproof, Tensas Parish: Tensas Parish Health Unit. Free; syphilis only.

Weeks Island, Iberia Parish: Iberia Parish Health Unit. Free; syphilis only.

Welsh, Jefferson Davis Parish: Jefferson Davis Parish Health Unit, Kleinman Bldg. Free; syphilis only.

White Castle, Iberville Parish: Iberville Parish Health Unit. Free; syphilis only.

Winnfield, Winn Parish: Winn Parish Health Unit. Free; syphilis only.

Winnsboro, Franklin Parish: Franklin Parish Health Unit. Free; syphilis only.

Wisner, Franklin Parish: Franklin Parish Health Unit. Free; syphilis only.

MAINE

Augusta, Kennebec Co.: State Venereal Disease Clinic, 283 Water St. Free; all venereal diseases.

Bangor, Penobscot Co.: State Venereal Disease Clinic, 162 French St. Free and pay or part-pay; all venereal diseases.

Bath, Sagadahoc Co.: Bath Health Center, Custom House. Free; all venereal diseases.

Belfast, Waldo Co.: State Venereal Disease Clinic, 5 Northport Ave. Part-pay; all venereal diseases.

Biddeford, York Co.: State Venereal Disease Clinic, 107 Main St. Free; all venereal diseases.

Bingham, Somerset Co.: State Venereal Disease Clinic. Free; all venereal diseases.

Calais, Washington Co.: Calais Hospital, 15 Church St. Part-pay; all venereal diseases.

Danforth, Washington Co.: State Venereal Disease Clinic. Free and pay; all venereal diseases.

Eastport, Washington Co.: Sypilis and Gonorrhea Clinic. Free; all venereal diseases.

Ellsworth, Hancock Co.: State Venereal Disease Clinic, 75 Main St. Free; all venereal diseases.

Grand Isle, Aroostook Co.: State Venereal Disease Clinic. Free; all venereal diseases.

Guilford, Piscataquis Co.: State Venereal Disease Clinic. Free; all venereal diseases.

Houlton, Aroostook Co.: State Venereal Disease Clinic, Market Square. Part-pay; all venereal diseases.

Island Falls, Aroostook Co.: State Venereal Disease Clinic. Free and pay or part-pay; all venereal diseases.

Lewiston, Androscoggin Co.:
State Venereal Disease Clinic, 82 Pine St. Free; all venereal diseases.
State Venereal Disease Clinic, 199 Lisbon St. Free; all venereal diseases.

Millinocket, Penobscot Co.: State Venereal Disease Clinic, 3 Highland Ave. Free and part-pay; all venereal diseases.

Old Town, Penobscot Co.: State Venereal Disease Clinic, 197 Centre St. Free and part-pay; all venereal diseases.

Portland, Cumberland Co.:
State Venereal Disease Clinic, 65 India St. Part-pay; all venereal diseases.
State Venereal Disease Clinic, Maine Eye and Ear Infirmary, 79 Bramhall St. Free; syphilis only.
State Venereal Disease Clinic, Maine General Hospital, 22 Arsenal St. Free; syphilis only.

Presque Isle, Aroostook Co.: State Venereal Disease Clinic, Main St. Free; all venereal diseases.

Rockland, Knox Co.: State Venereal Disease Clinic, 463 Main St. Free; all venereal diseases.

Rumford, Oxford Co.: State Venereal Disease Clinic, 5 Franklin St. Free and part-pay; all venereal diseases.

Sanford, York Co.: State Venereal Disease Clinic, 29 Winter St. Free; all venereal diseases.

Waterville, Kennebec Co.: State Venereal Disease Clinic, Sisters Hospital. Free; all venereal diseases.

Wilton, Franklin Co.: State Venereal Disease Clinic, Main St. Free; all venereal diseases.

Winthrop, Kennebec Co.: State Venereal Disease Clinic, 1 Western Ave. Free; all venereal diseases.

MARYLAND

Annapolis, Anne Arundel Co.:
Annapolis Clinic, Emergency Hospital. Free; all venereal diseases.
St. Margaret's Clinic, R. F. D. No. 2. Free; all venereal diseases.

Baltimore:
City Clinic No. 1, Municipal Bldg. (Adults only.) Free; syphilis only; gonorrhea in women.
City Clinic No. 2, Druid Health Center, 1313 Druid Hill Ave. (Male, Negro only.) Free; all venereal diseases.
City Clinic No. 3, 28 South Broadway. (White, male only.) Free; all venereal diseases.
City Clinic No. 4, 419 N. Bond St. (Negro, male only.) Free; all venereal diseases.
City Clinic No. 6, Congenital Syphilis and Family Clinic, 1313 Druid Hill Ave. (Negro only.) Free; syphilis only.
City Clinic No. 5 and No. 7, Druid Health Center, 1313 Druid Hill Ave. (Negro only.) Free; syphilis only.
Baltimore Eye, Ear and Throat Hospital, Eutaw Place and Lanvale St. Free; syphilis only.
Genito-urinary Dispensary, Johns Hopkins Hospital, Broadway and Monument St. (Male only.) Part-pay; gonorrhea only.
Johns Hopkins Hospital, Broadway and Monument St. Part-pay; syphilis only.

Baltimore—Continued.

Mercy Hospital, Calvert and Saratoga Sts. (Adults only.) Free and part-pay; all venereal diseases.

Robert Garrett Dispensary, 27 N. Carey St. (Children only.) Free; all venereal diseases.

St. Agnes Hospital, Caton St. and Wilkins Ave. (White, male only.) Free and pay or part-pay; all venereal diseases.

Sinai Hospital, Monument St. and Rutland Ave. (White only.) Free and pay or part-pay; all venereal diseases.

South Baltimore General Hospital, Light St. Free and part-pay; all venereal diseases.

West Baltimore General Hospital, Raynor Ave. and Dukeland St. (White only.) Pay; all venereal diseases.

Bel Air, Harford Co.: Harford Co. Health Department, Bel Air Clinic, Masonic Temple. Free; all venereal diseases.

Berlin, Worcester Co.: State Clinic, Health Center Bldg. Free; all venereal diseases.

Brunswick, Frederick Co.: State Clinic, Emergency Hospital, B. & O. R. R. Bldg. Free; all venereal diseases.

Cambridge, Dorchester Co.: State Clinic. Free; all venereal diseases.

Centreville, Queen Anne Co.: State Clinic. Free; all venereal diseases.

Chestertown, Kent Co.: State Clinic, County Health Department. Free; all venereal diseases.

Crisfield, Somerset Co.: State Clinic, Health Center Bldg. Free; all venereal diseases.

Cumberland, Allegany Co.: State Clinic, City Hall. Free; all venereal diseases.

Damascus, Montgomery Co.: State Clinic, New Elementary School. Free; all venereal diseases.

Dawsonville, Montgomery Co.: State Clinic, Dr. U. D. Nourse's Office. Free; all venereal diseases.

Denton, Caroline Co.: State Clinic, County Health Department. Free; all venereal diseases.

Easton, Talbot Co.: State Clinic, County Health Department. Free; all venereal diseases.

Eldersburg, Carroll Co.: Dr. Wm. H. Lawson's Office. Free; all venereal diseases.

Elkton, Cecil Co.: State Clinic, East High St. Free; all venereal diseases.

Ellicott City, Howard Co.: State Clinic, County Health Department. Free; all venereal diseases.

Federalsburg, Caroline Co.: State Clinic, Fire Hall. Free; all venereal diseases.

Frederick, Frederick Co.: State Clinic, County Health Department. Free; all venereal diseases.

Friendsville, Garrett Co.: State Clinic, Office of Dr. Eugene Greenwald. Free; all venereal diseases.

Grantsville, Garrett Co.: State Clinic, Health Center. Free; all venereal diseases.

Grayton, Charles Co.: State Clinic, Church Hall. Free; all venereal diseases.

Hagerstown, Washington Co.: State Clinic, County Health Department, King St. (Adults only.) (Same clinic, children only.) Free; all venereal diseases.

Havre de Grace, Harford Co.: State Clinic, Harford Co. Health Center. Free; all venereal diseases.

Hughesville, Charles Co.: State Clinic, Doctor F. D. Chappelear's Office. Free; all venereal diseases.

Hurlock, Dorchester Co.: State Clinic, Hurlock Laboratory. Free; all venereal diseases.

Hyattsville, Prince Georges Co.: State Clinic, County Service Bldg., Rhode Island Ave. Free; all venereal diseases.

Kent Narrows, Queen Annes Co.: State Clinic, Baxter's Office Bldg. (Open September to May of each year.) Free; all venereal diseases.

Kitzmiller, Garrett Co.: State Clinic, Dr. R. R. Sisson's Office. Free; all venereal diseases.

La Plata, Charles Co.: State Clinic, County Health Department. Free; all venereal diseases.

Laurel, Prince Georges Co.: State Clinic, Police Court Bldg., Montgomery St. Free; all venereal diseases.

Leonardtown, St. Marys Co.: State Clinic, County Health Department. Free; all venereal diseases.

Linden, Montgomery Co.: State Clinic, Colored School. Free; all venereal diseases.

Millington, Kent Co.: State Clinic, Dulin Bldg. Free; all venereal diseases.

Oakland, Garrett Co.: State Clinic, Office of Dr. E. I. Baumgartner. Free; all venereal diseases.

Owensville, Anne Arundel Co.: State Clinic, Health Center. Free; all venereal diseases.

Pasadena, Anne Arundel Co.: State Clinic, Magothy Health Center. Free; all venereal diseases.

Pocomoke City, Worcester Co.: State Clinic, Clinic Bldg., Cor. Willow St. and Clarke Ave. Free; all venereal diseases.

Pomonkey, Charles Co.: State Clinic, Elks Hall. Free; all venereal diseases.

Prince Frederick, Calvert Co.: State Clinic, County Hospital. Free; all venereal diseases.

Princess Anne, Somerset Co.: State Clinic, County Health Department. Free; all venereal diseases.

Rock Hall, Kent Co.: State Clinic, Clinic Room in Tucker Bldg. Free; all venereal diseases.

Rockville, Montgomery Co.: State Clinic, County Health Department. Free; all venereal diseases.

Salisbury, Wicomico Co.:

Dr. C. T. Fisher's Private Clinic, Cor. Church and North Division Sts. Pay; all venereal diseases.

State Clinic, 226 Lake St. Free; all venereal diseases.

Sharptown, Wicomico Co.: State Clinic, Colored School. Free; all venereal diseases.

Snow Hill, Worcester Co.: State Clinic, Odd Fellows Bldg. Free; all venereal diseases.

Sparrows Point, Baltimore Co.: State Clinic, Bethlehem Steel Co. Hospital. Free; all venereal diseases.

St. Michaels, Talbot Co.: State Clinic, Over Johnson's Drug store. Free; all venereal diseases.

Stevensville, Queen Annes Co.: State Clinic, Grollman's Bldg. Free; all venereal diseases.

Still Pond, Kent Co.: State Clinic, Colored School. Free; all venereal diseases.

Sudlersville, Queen Annes Co.: State Clinic, Redden Residence. Free; all venereal diseases.

Towson, Baltimore Co.: State Clinic, Health Department Bldg. Free; all venereal diseases.

Tyaskin, Wicomico Co.: State Clinic, Odd Fellows Hall. Free; all venereal diseases.

Upper Marlboro, Prince Georges Co.: State Clinic, County Health Department. Free; all venereal diseases.

Westernport, Allegany Co.: State Clinic, Reeves Hospital. Free; all venereal diseases.

Westminster, Carroll Co.: State Clinic, County Health Department, 3 East Main St. Free; all venereal diseases.

Wheaton, Montgomery Co.: State Clinic, Dr. Webster Sewell's Office. Free; all venereal diseases.

MASSACHUSETTS

(Clinics marked with asterisk have been designated as Cooperating Clinics)

***Beverly, Essex Co.:** Beverly Hospital, Herriek & Heather Sts. Free and pay or part-pay; syphilis and gonorrhea.

Boston, Suffolk Co.:

*Beth Israel Hospital, 330 Brookline Ave. Free and pay or part-pay; syphilis and gonorrhea.

*Boston City Hospital, 818 Harrison Ave. Free and pay or part-pay; syphilis and gonorrhea.

*Boston Dispensary, 25 Bennet St. Free and pay or part-pay; syphilis and gonorrhea.

Boston Psychopathic Hospital, 74 Fenwood Road. Free; neurosyphilis only.

*Children's Hospital, 300 Longwood Ave. (Children only.) Free and pay or part-pay; syphilis only.

*Massachusetts General Hospital, Fruit St. Free and pay or part-pay; syphilis and gonorrhea.

*Massachusetts Memorial Hospitals, 88 East Concord St. Free and pay or part-pay; syphilis and gonorrhea.

*Peter Bent Brigham Hospital, 721 Huntington Ave. Free and pay or part-pay; syphilis and gonorrhea.

***Brockton, Plymouth Co.:** Brockton Hospital, 680 Center St. Free and pay or part-pay; syphilis and gonorrhea.

Cambridge, Middlesex Co.:

*Cambridge Hospital, 330 Mount Auburn St. Free and pay or part-pay; syphilis only.

Cambridge City Hospital, 1493 Cambridge St. Free; syphilis and gonorrhea.

***Fall River, Bristol Co.:** Board of Health Clinic, City Hall Annex, Third St. Free and pay or part-pay; syphilis and gonorrhea.

***Fitchburg, Worcester Co.:** Burbank Hospital, Hospital Road. Free and pay or part-pay; syphilis and gonorrhea.

***Great Barrington, Berkshire Co.:** Fairview Hospital, Lewis Ave. Free and pay or part-pay; syphilis and gonorrhea.

***Haverhill, Essex Co.:** Board of Health Clinic, 471 Main St. Free and pay or part-pay; syphilis and gonorrhea.

*Holyoke, Hampshire Co.: Holyoke Hospital, Beech St. Free and pay or part-pay; syphilis and gonorrhea.

Lawrence, Essex Co.:

Board of Health Clinic, 130 Oak St. Free and pay or part-pay; syphilis and gonorrhea.

*Lawrence Clinic, 133 Methuen St. Free and pay or part-pay; syphilis and gonorrhea.

*Lowell, Middlesex Co.: Board of Health Clinic, Kirk and Paige Sts. Free and pay or part-pay; syphilis and gonorrhea.

*Lynn, Essex Co.: Lynn Hospital, 212 Boston St. Free and pay or part-pay; syphilis and gonorrhea.

*New Bedford, Bristol Co.: Board of Health Clinic, 519 Olympia Building. Free and pay or part-pay; syphilis and gonorrhea.

*Newton, Middlesex Co.: Newton Hospital, 2014 Washington St. Free and pay or part-pay; syphilis and gonorrhea.

*Pittsfield, Berkshire Co.: House of Mercy Hospital, 741 North St. Free and pay or part-pay; syphilis and gonorrhea.

Quincy, Norfolk Co.: Board of Health Clinic, Quincy Dispensary, High School Ave. Free; syphilis and gonorrhea.

Roxbury, Suffolk Co.: New England Hospital for Women and Children, Dimock St. Free and pay or part-pay; syphilis and gonorrhea.

*Springfield, Hampshire Co.: Springfield Hospital, 759 Chestnut St. Free and pay or part-pay; syphilis and gonorrhea.

Taunton, Bristol Co.: Board of Health Clinic, City Hall, Main St. Free; syphilis and gonorrhea.

*Waltham, Middlesex Co.: Waltham Hospital, Hope Ave. Free and pay or part-pay; syphilis and gonorrhea.

Worcester, Worcester Co.:

*The Memorial Hospital, 119 Belmont St. Free and pay or part-pay; syphilis and gonorrhea.

*Worcester City Hospital, 162 Chandler St. Free and pay or part-pay; syphilis and gonorrhea.

MICHIGAN

Battle Creek, Calhoun Co.: Battle Creek City Clinic, Room 8, City Hall, Michigan Ave. West. Free; all venereal diseases.

Benton Harbor, Berrien Co.: Benton Harbor Clinic. Free; syphilis and gonorrhea only.

Berrien Center, Berrien Co.: Berrien Center Clinic. Free; syphilis and gonorrhea only.

Dearborn, Wayne Co.: Dearborn Medical Center, 10149 Michigan Ave. Free; all venereal diseases.

Detroit, Wayne Co.:

Deaconess Hospital, 3245 East Jefferson Ave. Free and part-pay; all venereal diseases.

Grace Hospital, 268 East Willis Ave. Free and pay or part-pay; all venereal diseases.

Harper Hospital, 3825 Brush St. (Adults only.) Free and pay; all venereal diseases.

North End Clinic, 936 Holbrook St. Free and part-pay; all venereal diseases.

Detroit, Wayne Co.—Continued.
St. Joseph's Mercy Hospital, 2200 East Grand Blvd. Free; syphilis only.
Social Hygiene Clinic, 555 Clinton St. Free; all venereal diseases.

Eloise, Wayne Co.: Eloise Hospital Clinic. Free and part-pay; all venereal diseases.

Flint, Genesee Co.: Health Department Clinic, Hurley Hospital. Free; all venereal diseases.

Grand Rapids, Kent Co.: Social Hygiene Clinic, City Hall. Free; all venereal diseases.

Hamtramck, Wayne Co.: Venereal Clinic, 10036 Jos. Campau Ave. Free; all venereal diseases.

Highland Park, Wayne Co.: Highland Park General Hospital. Free; all venereal diseases.

Jackson, Jackson Co.: Jackson City Clinic, City Offices. Free; diagnostic only.

Kalamazoo, Kalamazoo Co.: Kalamazoo City Clinic, 241 W. South St. Free; all venereal diseases.

Lansing, Ingham Co.: Lansing City Clinic, 112½ W. Allegan St. Free; all venereal diseases.

Midland, Midland Co.: County Health Department Clinic, County Health Office. (White only.) Free; all venereal diseases.

Niles, Berrien Co.: Niles Clinic. Free; syphilis and gonorrhea only.

Pontiac, Oakland Co.:
City Diagnostic Clinic, 465 West Huron St. Diagnostic only.
Oakland Co. Clinic, 436 Auburn Ave. Free; all venereal diseases.

Royal Oak, Oakland Co.: Royal Oak Clinic, 111 South Troy St. Free; all venereal diseases.

Saginaw, Saginaw Co.: City Clinic, 130 East Bristol St. Free; all venereal diseases.

Wyandotte, Wayne Co.: Wyandotte Health Department, 839 Biddle Ave. (White only.) Free; all venereal diseases.

Ypsilanti, Washtenaw Co.: Social Hygiene Clinic, City Hall. Free; syphilis only.

MINNESOTA

Duluth, St. Louis Co.: City Venereal Disease Clinic, Hearding Hospital, 612 East Third St. Free; all venereal diseases.

Minneapolis, Hennepin Co.:
Lymanhurst Health Center (City Health Department V. D. Clinic), 1800 Chicago Ave. Free; all venereal diseases.
Minneapolis General Hospital, 619 South Fifth St. Free; all venereal diseases.
Minnesota General (University) Hospitals. Free and part-pay; all venereal diseases.
Wells Memorial Dispensary, 75½ Glenwood Ave. North. Part-pay; all venereal diseases.

Rochester, Olmsted Co.: City Venereal Disease Clinic, City Hall. Free; all venereal diseases.

St. Paul, Ramsey Co.:
Amherst H. Wilder Dispensary, 279 Rice St. Part-pay; all venereal diseases.
Ancker Hospital (City and County Hospital), Colborne St. and Jefferson Ave. Free; all venereal diseases.

Savage, Scott Co.: State Transient Camp (V. D. Clinic), Camp No. 3. (Male only.) Free; all venereal diseases.

MISSISSIPPI

Abbeville, Lafayette Co.: Lafayette Co. Health Department. Free; syphilis only.

Aberdeen, Monroe Co.: Monroe Co. Health Department, City Hall. Free; syphilis only.

Amory, Monroe Co.: Monroe Co. Health Department, City Hall. Free; syphilis only.

Anguilla, Sharkey Co.: Sharkey Co. Health Department. Free; syphilis only.

Arcola, Washington Co.: Washington Co. V. D. Clinic. Free; all venereal diseases.

Artesia, Lowndes Co.: Lowndes Co. Health Department. Free; syphilis only.

Baldwyn, Lee Co.: Caldwell's Clinic. Free; syphilis only.

Batesville, Panola Co.: Panola Co. Health Department. Free; syphilis only.

Bay Springs, Jasper Co.: Jasper Co. Health Department. Part-pay; syphilis only.

Beaumont, Perry Co.: Perry Co. Health Department. Free; syphilis only.

Belzoni, Humphreys Co.: Humphreys Co. Health Department, Courthouse. Free; syphilis only.

Benton, Yazoo Co.: Yazoo Co. Health Department. Free; syphilis only.

Bentonia, Yazoo Co.: Yazoo Co. Health Department, Colored Church. Free; syphilis only.

Brookhaven, Lincoln Co.: Lincoln Co. Health Department, Syphilis Clinic. Free; syphilis only.

Brookville, Noxubee Co.: Noxubee Co. Health Department, V. D. Clinic. Free; syphilis only.

Camden, Madison Co.: Madison Co. Health Department. Free; syphilis only.

Canton, Madison Co.: Madison Co. Health Department. Free; syphilis only.

Cary, Sharkey Co.: Sharkey Co. Health Department. Free; syphilis only.

Catchings, Sharkey Co.: Sharkey Co. Health Department. Free; syphilis only.

Charleston, Tallahatchie Co.: Tallahatchie Co. Health Department. Free; syphilis only.

Clarksdale, Coahoma Co.:

Coahoma Co. Health Department, Third St. (Negro only. White only on Mondays.) Part-pay; syphilis only.

Coahoma Co. Health Department, King & Anderson Plantation, Route 2. Part-pay; syphilis only.

Cleveland, Bolivar Co.: Bolivar Co. Health Department. Free; syphilis only.

Coldwater, Tate Co.: Tate Co. Health Department. Free; syphilis only.

Columbia, Marion Co.: Marion Co. Health Department. Free; syphilis only.

Columbus, Lowndes Co.: Lowndes Co. Health Department. Free; syphilis only.

Como, Panola Co.: Panola Co. Health Department. Free; syphilis only.

Corinth, Alcorn Co.: Alcorn Co. Health Department, Franklin St. (Tuesdays, Negro only. Mondays, White only. Wednesdays, both.) Free; syphilis only.

Crenshaw, Panola Co.: Panola Co. Health Department. Free; syphilis only.

Cruger, Holmes Co.: Holmes Co. Health Department, Main St. Free; syphilis only.

Doddsville, Sunflower Co.: Sunflower Co. Health Department. Free; all venereal diseases.

Drew, Sunflower Co.: Sunflower Co. Health Department. Free; syphilis only.
Dubbs, Tunica Co.: Tunica Co. Health Department. Pay; syphilis only.
Dublin, Coahoma Co.: Coahoma Co. Health Department. Part-pay; syphilis only.
Duncan, Bolivar Co.: Bolivar Co. Health Department. Free; syphilis only.
Dundee, Tunica Co.: Tunica Co. Health Department. Pay; syphilis only.
Ebenezer, Holmes Co.: Holmes Co. Health Department, Route 4. Free; syphilis only.
Edwards, Hinds Co.: Hinds Co. Health Department. Free; syphilis only.
Ellisville, Jones Co.: Jones Co. Health Department. Free; syphilis only.
Evansville, Tunica Co.: Tunica Co. Health Department. Pay; syphilis only.
Fitler, Issaquena Co.: Issaquena Co. Health Department, Health Center. Free; syphilis only.
Flora, Madison Co.: Madison Co. Health Department. Free; syphilis only.
Friars Point, Coahoma Co.: Coahoma Co. Health Department. Part-pay; syphilis only.
Georgetown, Copiah Co.: Copiah Co. Health Department. Part-pay; syphilis only.
Glen Allen, Washington Co.: Washington Co. Health Department. Free; all venereal diseases.
Glendora, Tallahatchie Co.: Tallahatchie Co. Health Department. Free; syphilis only.
Gloster, Amite Co.: Amite Co. Health Department. Free; syphilis only.
Grace, Issaquena Co.: Issaquena Co. Health Department. Free; syphilis only.
Greenville, Washington Co.: Washington Co. Health Department, North Harvey St. Free; all venereal diseases.
Greenwood, Leflore Co.: Leflore Co. Health Department. Free; syphilis only.
Gunnison, Bolivar Co.: Bolivar Co. Health Department. Free; syphilis only.
Hattiesburg, Forrest Co.: Forrest Co. Health Department, Courthouse. Free; all venereal diseases.
Hazlehurst, Copiah Co.: Copiah Co. Health Department. Part-pay; syphilis only.
Hernando, De Soto Co.: De Soto Co. Health Department. Part-pay; syphilis only.
Hollandale, Washington Co.: Washington Co. Health Department. Free; all venereal diseases.
Holly Bluff, Yazoo Co.: Yazoo Co. Health Department. Free; syphilis only.
Holly Springs, Marshall Co.: Marshall Co. Health Department. Free; syphilis only.
Indianola, Sunflower Co.: Sunflower Co. Health Department. Free; all venereal diseases.
Inverness, Sunflower Co.: Sunflower Co. Health Department. Free; all venereal diseases.
Isola, Humphreys Co.: Humphreys Co. Health Department, Mayor's Office. Free; syphilis only.
Itta Bena, Leflore Co.: Leflore Co. Health Department, Route 2. Free; syphilis only.
Luka, Tishomingo Co.: Tishomingo Co. Health Department. Part-pay; syphilis only.
Jackson, Hinds Co.: Hinds Co. Health Department. Free; syphilis only.
Jonestown, Coahoma Co.: Coahoma Co. Health Department. Party-pay; syphilis only.
Lake Cormorant, De Soto Co.: De Soto Co. Health Department. Part-pay; syphilis only.

Lauderdale, Lauderdale Co.: Lauderdale Co. Health Department. Dr. M. L McKinnon's Office. Free; syphilis only.

Laurel, Jones Co.: Jones Co. Health Department. Free; syphilis and gonorrhea only.

Leaf, Greene Co.: Greene Co. Health Department. Free; syphilis only.

Leakesville, Greene Co.: Greene Co. Health Department. Free; syphilis only.

Leland, Washington Co.: Washington Co. Health Department. Free; all venereal diseases.

Liberty, Amite Co.: Amite Co. Health Department. Free; syphilis only.

Lombardy, Sunflower Co.: Sunflower Co. Health Department. Free; all venereal diseases.

Louise, Humphreys Co.: Humphreys Co. Health Department, Dr. J. N. Mecklin's Office. Free; syphilis only.

Lucedale, George Co.: George Co. Health Department. Free; syphilis only.

Lula, Coahoma Co.: Coahoma Co. Health Department. Part-pay; syphilis only.

Macon, Noxubee Co.: Noxubee Co. Venereal Disease Clinic. Free; syphilis only.

Magnolia, Pike Co.: Pike Co. Health Department, Health Center. Free; syphilis only.

McComb, Pike Co.: Pike Co. Health Department, Health Center. Free; syphilis only.

McLain, Greene Co.: Greene Co. Health Department. Free; syphilis only.

Meridian, Lauderdale Co.: Lauderdale Co. Health Department, 1319 23d Ave. Part-pay; all venereal diseases.

Marigold, Bolivar Co.: Bolivar Co. Health Department. Free; syphilis only.

Mileston, Holmes Co.: Holmes Co. Health Department. Free; syphilis only.

Minter City, Leflore Co.: Leflore Co. Health Department. Free: syphilis only.

Money, Leflore Co.: Leflore Co. Health Department. Free; syphilis only.

Moorhead, Sunflower Co.: Sunflower Co. Health Department. Free; all venereal diseases.

Myrtle, Union Co.: Union Co. Health Department. Free and part-pay; syphilis only.

Natchez, Adams Co.: Adams Co. Health Department, Municipal Bldg., Pearl St. Free; syphilis only.

Nettleton, Lee Co.: Lee Co. Health Department, Dr. J. T. Dabb's Office. Free; syphilis only.

New Albany, Union Co.: Union Co. Health Department, 305 Main St. Free and part-pay; syphilis only.

Nitta Yuma, Sharkey Co.: Sharkey Co. Health Department. Free; syphilis only.

Olive Branch, De Soto Co.: De Soto Co. Health Department. Part-pay; syphilis only.

Osyka, Pike Co.: Osyka Syphilis Clinic, Health Office. Free; syphilis only.

Oxford, Lafayette Co.: Lafayette Co. Health Department. Free; syphilis only.

Pace, Bolivar Co.: Bolivar Co. Health Department. Free; syphilis only.

Paulette, Noxubee Co.: Noxubee Co. Health Department. Free; syphilis only.

Picayune, Pearl River Co.: Pearl River Co. Health Department. Part-pay; syphilis and gonorrhea.

Plantersville, Lee Co.: Lee Co. Health Department, Dr. Cantrell's Office. Free; syphilis only.

Pocahontas, Hinds Co.: Hinds Co. Health Department. (Adults only.) Free; syphilis only.

Poplarville, Pearl River Co.: Pearl River Co. Health Department. Part-pay; syphilis and gonorrhea.
Raleigh, Smith Co.: Smith Co. Health Department. Part-pay; syphilis only.
Raymond, Hinds Co.: Hinds Co. Health Department. Free; syphilis only.
Robinsonville, Tunica Co.: Tunica Co. Health Department. Pay; syphilis only.
Rochdale, Bolivar Co.: Bolivar Co. Health Department. Free; syphilis only.
Rolling Fork, Sharkey Co.: Sharkey Co. Health Department. Free; syphilis only.
Rosedale, Bolivar Co.: Bolivar Co. Health Department. Free; syphilis only.
Roundaway, Coahoma Co.: Coahoma Co. Health Department. Part-pay; syphilis only.
Ruleville, Sunflower Co.: Sunflower Co. Health Department. Free; all venereal diseases.
Scott, Bolivar Co.: Bolivar Co. Health Department. Free; syphilis only.
Senatobia, Tate Co.: Tate Co. Health Department. Free; syphilis only.
Shannon, Lee Co.: Lee Co. Health Department, Dr. Cowden's Office. Free; syphilis only.
Shaw, Bolivar Co.: Bolivar Co. Health Department. Free; syphilis only.
Shelby, Bolivar Co.: Bolivar Co. Health Department. Free; syphilis only.
Shellmound, Leflore Co.: Leflore Co. Health Department. Free syphilis only.
Sherard, Coahoma Co.: Coahoma Co. Health Department. (Negro only.) Part-pay; syphilis only.
Shuqualak, Noxubee Co.: Noxubee Co. Health Department. Free; syphilis only.
Silver City, Humphreys Co.: Humphreys Co. Health Department, Dr. G. S. Bryan's Office. Free; syphilis only.
Soso, Jones Co.: Jones Co. Health Department. Free; syphilis only.
Sumner, Tallahatchie Co.: Tallahatchie Co. Health Department. Free; syphilis only.
Sunflower, Sunflower Co.: Sunflower Co. Health Department. Free; all venereal diseases.
Swiftown, Leflore Co.: Leflore Co. Health Department. Free; syphilis only.
Taylor, Lafayette Co.: Lafayette Co. Health Department. Free; syphilis only.
Thyatira, Tate Co.: Tate Co. Health Department. Free; syphilis only.
Tunica, Tunica Co.: Tunica Co. Health Department. Pay; syphilis only.
Tupelo, Lee Co.:
Lee Co. Health Department. Free; all venereal diseases.
North Mississippi Community, Hospital Clinic. Free; syphilis only.
Utica, Hinds Co.: Hinds Co. Health Department. Free; syphilis only.
Valley, Yazoo Co.: Yazoo Co. Health Department. Free; syphilis only.
Valley Park, Issaquena Co.: Issaquena Co. Health Department. Free; syphilis only.
Vicksburg, Warren Co.: Warren Co. Health Department. Free; all venereal diseases.
Walls, De Soto Co.: De Soto Co. Health Department. Part-pay; syphilis only.
Wesson, Copiah Co.: Copiah Co. Health Department. Part-pay; syphilis only.
Wiggins, Stone Co.: Stone Co. Health Department. Free; syphilis only.
Yazoo City, Yazoo Co.: Yazoo Co. Health Department. Free; syphilis only.

MISSOURI

Aurora, Lawrence Co.: Southwestern Missouri V. D. Clinic, City Hall. Free; all venereal diseases.

Ava, Douglas Co.: Douglas Co. Venereal Clinic. Part-pay; all venereal diseases.
Benton, Scott Co.: Benton Venereal Disease Clinic, County Courthouse. Free; all venereal diseases.
Butler, Bates Co.: Butler V. D. Clinic, Courthouse. Free; all venereal diseases.
Cameron, Clinton Co.: Cameron Clinic. Free; all venereal diseases.
Canton, Lewis Co.: Venereal Disease Clinic, Office of Dr. P. W. Jennings. Free; all venereal diseases.
Cape Girardeau, Cape Girardeau Co.: Cape Girardeau Venereal Disease Clinic, Cahoon Building, Spanish & Broadway. Free; all venereal diseases.
Carthage, Jasper Co.: Southwestern Missouri V. D. Clinic, Benton School. Free; all venereal diseases.
Caruthersville, Pemiscot Co.: Pemiscot Co. Clinic. Free; all venereal diseases.
Cassville, Barry Co.: Venereal Disease Clinic, Barry County Hospital. Free; all venereal diseases.
Charleston, Mississippi Co.: Charleston Venereal Disease Clinic, Courthouse. Free; all venereal diseases.
Clayton, St. Louis Co.: Venereal Disease Clinic. Free; all venereal diseases.
Dexter, Stoddard Co.: Dexter Clinic. Free; all venereal diseases.
Doniphan, Ripley Co.: Venereal Disease Clinic, Courthouse. Free; all venereal diseases.
East Prairie, Mississippi Co.: East Prairie Venereal Disease Clinic, Mobile Unit. Free; all venereal diseases.
Eldon, Miller Co.: Dr. Shelton's Clinic, 6 South Maple St. Part-pay; all venereal diseases.
Fredericktown, Madison Co.: Syphilis Clinic, 126 West Main St. Free; all venereal diseases.
Fulton, Callaway Co.: Venereal Disease Clinic, Courthouse. Free; all venereal diseases.
Greenville, Wayne Co.: Greenville Clinic, Courthouse. Free; all venereal diseases.
Hannibal, Marion Co.: Venereal Clinic, Courthouse. Free; all venereal diseases.
Harrisonville, Cass Co.: Harrisonville V. D. Clinic, 106a East Pearl St. Free; all venereal diseases.
Higginsville, Lafayette Co.: Public Health Clinic, Russell and Patrick Sts. Free; all venereal diseases.
Jefferson City, Cole Co.: Venereal Disease Clinic, 234 Madison St. Free; all venereal diseases.
Joplin, Jasper Co.: Southwestern Missouri V. D. Clinic, City Hall. Free; all venereal diseases.
Kansas City, Jackson Co.:

Alfred Benjamin Dispensary, 1000 Admiral Blvd. Free and part-pay; all venereal diseases.
Children's Mercy Hospital, 1710 Independence Ave. (White children only.) Free; syphilis only.
General Hospital, 24th and Cherry Sts. (White only.) Free; all venereal diseases.
General Hospital, 600 East 22nd St. (Negro only.) Free; all venereal diseases.
Good Shepherd Clinic. (Women and children only.) Free; all venereal diseases.
Municipal Tuberculosis Hospital, Leeds Station. Free; syphilis only.
West Side Health Center, 721 West 18th St. Part-pay; all venereal diseases.

Kansas City, Jackson Co.—Continued.

Wheatley Hospital, 1826 Forest Ave. Part-pay; all venereal diseases.

Women's Reformatory, Leeds Station. (Female only.) Free; all venereal diseases.

Kennett, Dunklin Co.: Kennett V. D. Clinic. Free; all venereal diseases.

Koch, St. Louis Co.: Robert Koch Hospital. Free; all venereal diseases.

Lebanon, Laclede Co.: Lebanon V. D. Clinic, Office of Dr. J. A. McComb. Free and part-pay; all venereal diseases.

Little Blue, Jackson Co.: Jackson Co. Hospital. (White only.) Free; all venereal diseases.

Malden, Dunklin Co.: Malden Venereal Disease Clinic. Free; all venereal diseases.

Marble Hill, Bollinger Co.: Syphilis Clinic, Main St. Free; all venereal diseases.

Marceline, Linn Co.: Marceline Clinic, East Howell St. Free; all venereal diseases.

Mexico, Audrain Co.: Mexico Clinic, 101 North Western St. Part-pay; all venereal diseases.

Monette, Barry Co.: Venereal Disease Clinic, District Health Office. Free; all venereal diseases.

Mt. Vernon, Lawrence Co.: Southwestern Missouri V. D. Clinic, County Courthouse. Free; all venereal diseases.

Neosho, Newton Co.: Southwestern Missouri V. D. Clinic, Old City Jail Building. Free; all venereal diseases.

New Madrid, New Madrid Co.: New Madrid Co. Clinic. Free; syphilis only.

Osceola, St. Clair Co.: Osceola V. D. Clinic, Public Health Office. Free and part-pay; all venereal diseases.

Owensville, Gasconade Co.: Health Office Clinic. (White only.) Free; all venereal diseases.

Platte City, Platte Co.: Platte Co. Clinic. Free; all venereal diseases.

Pleasant Hill, Cass Co.: Pleasant Hill V. D. Clinic, City Hall. Free; all venereal diseases.

Poplar Bluff, Butler Co.: Poplar Bluff V. D. Clinic, County Courthouse. Free; all venereal diseases.

Portageville, New Madrid Co.: Portageville Clinic. Free; all venereal diseases.

St. Joseph, Buchanan Co.: Venereal Disease Clinic, Community Hall. Free; all venereal diseases.

St. Louis, St. Louis Co.:

Alexian Brothers' Hospital, 3933 South Broadway. (White only.) Free; all venereal diseases.

City Hospital No. 1, 14th and Lafayette Sts. (White only.) Free; all venereal diseases.

City Isolation Hospital, 5600 Arsenal St. Free and part-pay; syphilis only.

City Sanitarium, 5400 Arsenal St. (Adults only.) Free; all venereal diseases.

City Special Hospital, 4200 South Broadway. (Female only.) Free; all venereal diseases.

Convent of the Good Shepherd, 3801 Gravois St. (Female only.) Free; all venereal diseases.

Firmin Desloge Hospital, 1325 South Grand St. Free and part-pay; all venereal diseases.

Homer G. Phillips, 2601 North Whittier St. (Negro only.) Free; all venereal diseases.

St. Louis, St. Louis Co.—Continued.

Jewish Hospital, 216 South Kingshighway. (White only.) Free and pay or part-pay; all venereal diseases.

Municipal Venereal Disease Clinic, 18 Municipal Courts Bldg., 14th and Market Sts. Free; all venereal diseases.

St. John's Dispensary, 4945 Audubon Ave. (White only.) Free and pay or part-pay; all venereal diseases.

St. Mary's Infirmary, 1536 Papin St. (Negro only.) Free; all venereal diseases.

Washington University Clinics, 507 South Euclid Ave. Part-pay; all venereal diseases.

Salem, Dent Co.: Venereal Disease Clinic, Old Community Building. Free; all venereal diseases.

Sedalia, Pettis Co.: Public Health Clinic, Old Y. M. C. A. Building, 5th and Lamine Sts. Free; all venereal diseases.

Sikeston, Scott Co.: Sikeston V. D. Clinic, Health Office, City Hall. Free; all venereal diseases.

Springfield, Greene Co.: Greene Co. Venereal Disease Clinic, Courthouse. Free; all venereal diseases.

Steelville, Crawford Co.: Venereal Disease Clinic, Social Security Bldg. Free; all venereal diseases.

Thompson's Bend, Mississippi Co.: Thompson's Bend V. D. Clinic, Mobile Unit. Free; all venereal diseases.

Trailback Plantation, Dunklin Co.: Trailback Plantation Clinic. Free; all veneral diseases.

Trenton, Grundy Co.: Venereal Disease Clinic, 905½ Main St. Free; all venereal diseases.

Tuscumbia, Miller Co.: Health Department, Courthouse. Free; all venereal diseases.

Warrensburg, Johnson Co.: Public Health Clinic, 217½ North Holden St. Free; all venereal diseases.

Washington, Franklin Co.: Franklin Co. (and surrounding vicinity), 115 Elm St. Free; all venereal diseases.

Waynesville, Pulaski Co.: Venereal Diseases Clinic, Old Bank Bldg. Free; all venereal diseases.

Webb City, Jasper Co.: Jasper Co. Health Department Clinic, 115 North Madison St. Free; all venereal diseases.

West Plains, Howell Co.: Venereal Disease Clinic, Dr. E. Royse Bohrer's Office, 111 West Main St. Free; all venereal diseases.

Wolf Island, Mississippi Co.: Wolf Island Venereal Disease Clinic, Mobile Unit. Free; all venereal diseases.

Wyatt, Mississippi Co.: Wyatt Venereal Disease Clinic, Mobile Unit. Free; all venereal diseases.

MONTANA

Bozeman, Gallatin Co.: City-County Health Office, Courthouse. Free; all venereal diseases.

Great Falls, Cascade Co.: City-County Health Department, Civic Center Bldg. Free; all venereal diseases.

NEBRASKA

Grand Island, Hall Co.: Local V. D. Clinic, 218 North Locust St. Free; all venereal diseases.

Hastings, Adams Co.: Adams Co. V. D. Clinic, Madgett Bldg. Free and pay or part-pay; all venereal diseases.

Lincoln, Lancaster Co.: Lincoln City Clinic, 935 R St. Free; all venereal diseases.

Norfolk, Madison Co.: Diagnostic and Treatment Center, 106 South 4th St. Free; all venereal diseases.

North Platte, Lincoln Co.: Diagnostic and Treatment Center, 517½ North Dewey St. Free; all venereal diseases.

Omaha, Douglas Co.:

City Venereal Clinic, 912 Douglas St. (Female only.) Free; all venereal diseases.

Creighton Medical Dispensary, 14th and Davenport Sts. Free and part-pay; all venereal diseases.

Douglas Co. Hospital, 40th and Poppleton Sts. Free; all venereal diseases.

University of Nebraska Dispensary, 42d St. and Dewey Ave. Free and part-pay; all venereal diseases.

Scottsbluff, Scottsbluff Co.: Diagnostic and Treatment Center, 1602 Broadway. Free; all venereal diseases.

NEVADA

Reno, Washoe Co.: Washoe Co. Venereal Disease Clinic, Washoe General Hospital. Part-pay; all venereal diseases.

NEW HAMPSHIRE

Berlin, Coos Co.: Venereal Disease Clinic, St. Louis Hospital, 459 Main St. Free; all venereal diseases.

Concord, Merrimack Co.: Venereal Disease Clinic, 5 Warren St. Free; all venereal diseases.

Dover, Strafford Co.: Venereal Disease Clinic, 90 Washington St. Free; all venereal diseases.

Manchester, Hillsboro Co.: Venereal Disease Clinic, Elliot Hospital, 955 Auburn St. Free; all venereal diseases.

Nashua, Hillsboro Co.: Venereal Disease Clinic, 184 Main St. Free; all venereal diseases.

Portsmouth, Rockingham Co.: Venereal Disease Clinic, Portsmouth Hospital. Free; all venereal diseases.

NEW JERSEY

Asbury Park, Monmouth Co.: Shore Regional Clinic, 109 Atkins Ave. Free; syphilis only.

Atlantic City, Atlantic Co.: Municipal Hospital, 900 Adriatic Ave. Free; all venereal diseases.

Bayonne, Hudson Co.: Bayonne Hospital, East 30th St. Free; all venereal diseases.

Belvidere, Warren Co.: Dr. N. C. Marlett's Office, 309 Front St. Free; syphilis only.

Blairstown, Warren Co.: Dr. W. R. Bostwick's Office, Main St. Free; syphilis only.

Bloomfield, Essex Co.: Essex Co. Health Department, Municipal Bldg. Free; syphilis and gonorrhea only.

Boonton, Morris Co.: Boonton Clinic, 311 West Main St. Free; all venereal diseases.

Bordentown, Burlington Co.: Bordentown V. D. Clinic, 412 Farnsworth Ave. Free; all venereal diseases.

Bound Brook, Somerset Co.: Bound Brook Hospital, 507 Church St. Free; all venereal diseases.

Branchville, Sussex Co.: Dr. F. H. Lushear's Office, Main St. Free; syphilis only.

Bridgeton, Cumberland Co.: Bridgeton Hospital. Free; all venereal diseases.

Burlington, Burlington Co.: Burlington District Clinic, V. D. Control, City Hall, High St. Free; all venereal diseases.

Camden, Camden Co.:

Cooper Hospital, 6th and Stevens Sts. Free and part-pay; all venereal diseases.

West Jersey Homeopathic Hospital, Mt. Ephraim and Atlantic Aves. Free and part-pay; syphilis only.

Carteret, Middlesex Co.: Venereal Clinic, Dr. Kemeny's Office, 48 Pulaski Ave. Free; all venereal diseases.

Cranbury, Middlesex Co.: Cranbury Clinic, Old Hightstown Road. Free; syphilis only.

Dover, Morris Co.: Regional Treatment Clinic, Dr. Hogan's Office, 29 East Blackwell St. Free; all venereal diseases.

Eatontown, Monmouth Co.: Eatontown Health Center, South St. (Negro only.) Free; syphilis only.

Elizabeth, Union Co.:

Alexian Brothers Hospital, 655 East Jersey St. Free; all venereal diseases.

Elizabeth General Hospital, Reid and E. Jersey Sts. Free; all venereal diseases.

St. Elizabeth Hospital, 204 South Broad St. Free; all venereal diseases.

Englewood, Bergen Co.: Venereal Clinic, Englewood Hospital, Engle St. Pay; all venereal diseases.

Franklin, Sussex Co.: Dr. L. B. Drake's Office, 47 Main St. Free; syphilis only.

Freehold, Monmouth Co.:

County Jail Clinic, Courthouse, Lafayette Place. (Adults only.) Free; syphilis only.

Freehold Clinic, M. C. O. S. S. Health Center, Lafayette Place. Free; syphilis only.

Hackensack, Bergen Co.: Hackensack Hospital, Hospital Place. Free and part-pay; all venereal diseases.

Hackettstown, Warren Co.: Dr. Carl A. Maxwell's Office, 117 Grand Ave. Free and pay or part-pay; all venereal diseases.

Hammonton, Atlantic Co.: Regional Health Commission, 108 Bellevue Ave. Free; all venereal diseases.

Hightstown, Mercer Co.: V. D. Clinic, 302 South Main St. (Negro only.) Free; syphilis only.

Irvington, Essex Co.: Municipal Hospital, 832 Chancellor Ave. Free; all venereal diseases.

Jersey City, Hudson Co.:

Christ Hospital, 176 Palisade Ave. Part-pay; all venereal diseases.

Medical Center, Montgomery St. and Baldwin Ave. Free and part-pay; all venereal diseases.

Kearny (Arlington), Hudson Co.: Hudson Co. Clinic, 753 Kearny Ave. Free; all venereal diseases.

Keyport, Monmouth Co.: Health Center, Main St. Free; syphilis only.

Long Branch, Monmouth Co.:

Monmouth Memorial Hospital, 3d Ave. Part-pay; all venereal diseases.

Night Clinic, Health Center, 65 Fourth Ave. Free; syphilis only.

Madison, Morris Co.: Madison Regional Health Commission Venereal Clinic, 1 Madison Ave. Part-pay; all venereal diseases.

Mahwah, Bergen Co.: Health Center, Valley Road, Hohokus Township. Free; syphilis only.

Manasquan, Monmouth Co.: Health Center, 67 Main St. Free; syphilis only.

Mays Landing, Atlantic Co.: Regional Health Commission, Courthouse. Free; syphilis only.

Millville, Cumberland Co.: Millville Clinic, 328 North 2d St. Free; all venereal diseases.

Montclair, Essex Co.: Mountainside Hospital, Bay Ave. Free and pay or part-pay; all venereal diseases.

Moorestown, Burlington Co.: Community House, 16 East Main St. Free; all venereal diseases.

Morristown, Morris Co.:

Memorial Hospital, 66 Morris Ave. Part-pay; all venereal diseases.

Regional Health Treatment Center, Water St. Free; all venereal diseases.

Neptune, Monmouth Co.: Fitkin Memorial Hospital. Free and part-pay; all venereal diseases.

Newark, Essex Co.:

Community Hospital, 132 West Kinney St. (White only.) Pay; syphilis only.

Health Department, Arlington and William Sts. Free; all venereal diseases.

Newark Beth Israel Hospital Clinic, 201 Lyons Ave. Free and pay or part-pay; all venereal diseases.

New Brunswick, Middlesex Co.: Middlesex General Hospital, Somerset St. Free; all venereal diseases.

New Monmouth, Monmouth Co.: Middletown Health Center, Campbell's Junction. Free; all venereal diseases.

Newton, Sussex Co.: Dr. E. K. Hawke's Office, 113 Main St. Free; syphilis only.

Northfield, Atlantic Co.: Atlantic Co. Hospital for Mental Diseases, Dolphin and Shore Roads. Free; syphilis only.

North Wildwood, Cape May Co.: Public Health Commission, Dr. Mace's Hospital, 2410 Atlantic Ave. Free; all venereal diseases.

Nutley, Essex Co.: Social Hygiene Clinic, Department of Health, 226 Chestnut St. Free; all venereal diseases.

Ogdensburg, Sussex Co.: Dr. H. M. Aitken's Office. Free; syphilis only.

Orange, Sussex Co.: Orange Memorial Hospital, 188 South Essex Ave. Free; all venereal diseases.

Passaic, Passaic Co.:

Beth Israel Hospital, 141 Madison St. Free and part-pay; all venereal diseases.

General Hospital, Lafayette Ave. Free; all venereal diseases.

Passaic, Passaic Co.—Continued.

St. Mary's Hospital, 211 Pennington Ave. Part-pay; syphilis only (separate clinic for gonorrhea).

Passaic, Passaic Co.:

Barnert Memorial Hospital, 30th St. and Broadway. Free and pay or part-pay; all venereal diseases.

Board of Health, Mill and Passaic Sts. Free; all venereal diseases.

Paterson General Hospital, Market St. and Madison Ave. Free and pay (when possible); all venereal diseases.

St. Joseph's Hospital, 703 Main St. Part-pay; all venereal diseases.

Penns Grove, Salem Co.: Old Moose Hall, South Broad St. and Mitchell Ave. Free; all venereal diseases.

Phillipsburg, Warren Co.: Warren Hospital, 845 Wilbur Ave. Free; all venereal diseases.

Plainfield, Union Co.: Muhlenburg Hospital, Park Ave. and Randolph Road. Part-pay; all venereal diseases.

Port Norris, Cumberland Co.: Shell Pile Clinic. Free; syphilis only.

Princeton, Mercer Co.: Princeton Hospital, Witherspoon St. Free; all venereal diseases.

Red Bank, Monmouth Co.:

Dr. M. J. Lorenzo's Office, 75 Riverside Ave. (White only.) Free and part-pay; syphilis only.

Red Bank Venereal Clinic, 131 Pearl St. (Negro only.) Free; syphilis only.

Riverside, Burlington Co.: West Burlington Co. Health Council, Zurbrugg Memorial Hospital, Taylor St. Free; syphilis only.

Roselle, Union Co.:

Dr. C. C. Polk's Office, 114 East 7th Ave. Free; all venereal diseases.

Dr. F. Glassnar's Office, 308 Chestnut St. Free; all venereal diseases.

Salem, Salem Co.: Salem Co. Memorial Hospital, New Market St. Free; all venereal diseases.

Somers Point, Atlantic Co.: Atlantic Shore Hospital, Sunny Ave. Free; all venereal diseases.

Somerville, Somerset Co.: Somerset Hospital, Rehill Ave. Free and pay; all venereal diseases.

Sparta, Sussex Co.: Dr. J. E. Longneeker's Office, Woodport Road. Free; all venereal diseases.

Summit, Union Co.: Summit Board of Health, 71 Summit Ave. Free; all venereal diseases.

Sussex, Sussex Co.: Dr. L. R. Eddy's Office, 40 Bank St. Free; all venereal diseases.

Teaneck, Bergen Co.: Holy Name Hospital, Teaneck Road. Part-pay; all venereal diseases.

Trenton, Mercer Co.:

McKinley Memorial Hospital, Brunswiek Ave. Part-pay; all venerea. diseases.

Venereal Clinic, Municipal Building, East State St. Free; all venereal diseases.

Vineland, Cumberland Co.: Newcomb Hospital, South State St. Free; all venereal diseases.

Washington, Warren Co.: Dr. W. H. Varney's Office, 122 Belvidere Ave. Free; syphilis only.

Weehawken, Hudson Co.: North Hudson Hospital, Park Ave. Part-pay; all venereal diseases.

Woodbine, Cape May Co.: V. D. Commission, State Colony Hospital, De Hirsch Ave. Free; all venereal diseases.

Woodbury, Gloucester Co.: Underwood Hospital, Broad St. and Red Bank Ave. Free; all venereal diseases.

NEW MEXICO

Albuquerque, Bernalillo Co.: Clinic Center, Courthouse. Free; all venereal diseases.

Belen, Valencia Co.: Belen Clinic. Free; syphilis only.

Bernalillo, Sandoval Co.: Sandoval Co. Health Department. Free; all venereal diseases.

Clovis, Curry Co.: Curry Co. V. D. Clinic, Courthouse. Free; all venereal diseases.

Deming, Luna Co.: Luna Co. Clinic, Courthouse Building. Free; all venereal diseases.

Espanola, Rio Arriba Co.: Venereal Disease Clinic. Free; all venereal diseases.

Gallup, McKinley Co.: Social Hygiene Clinic, McKinley Co. Health Department. Free; all venereal diseases.

Las Vegas, San Miguel Co.: Health Department Clinic, Romero Block. Free; syphilis only.

Lordsburg, Hidalgo Co.: Hidalgo Co. Clinic, Courthouse Building. Free; all venereal diseases.

Los Lunas, Valencia Co.: Los Lunas Clinic, Health Department. Free; syphilis only.

Pecos, San Miguel Co.: Health Department Clinic. Free; syphilis only.

Raton, Colfax Co.: Raton Clinic, County Courthouse. Free; all venereal diseases.

Santa Fe, Santa Fe Co.: Catholic Clinic, Cathedral Place. Free; all venereal diseases.

NEW YORK

Albany, Albany Co.:

Albany Hospital, New Scotland Ave. Free and part-pay; all venereal diseases.

Memorial Hospital, 714 Broadway. Free and part-pay; all venereal diseases.

St. Peter's Hospital, New Scotland Ave. Free; all venereal diseases.

Amsterdam, Montgomery Co.: Amsterdam Clinic, City Hall. Free; all venereal diseases.

Angola, Erie Co.: Physican's Office, 158 Main St. Free; all venereal diseases.

Auburn, Cayuga Co.: Social Hygiene Clinic, Auburn City Hospital. Free; all venereal diseases.

Bath, Steuben Co.: Bath Memorial Hospital, 115 East Steuben St. Free; all venereal diseases.

Beacon, Dutchess Co.: Beacon Syphilis Clinic, 453 Main St. Free; all venereal diseases.

Binghamton, Broome Co.: Health Department, 71 Collier St. Free; all venereal diseases.

Buffalo, Erie Co.:

Buffalo Columbus Hospital, 298–310 Niagara St. Free and part-pay; all venereal diseases.

Buffalo General Hospital, 100 High St. Part-pay; syphilis only.

Emergency Hospital, 108 Pine St. Free; syphilis only.

Mercy Hospital, 1365 Abbott Road. Free; syphilis only.

Meyer Memorial Hospital, 462 Grider St. Part-pay; syphilis only.

Millard Fillmore Hospital, 875 Lafayette Ave. (Adults only.) Free; all venereal diseases.

Swan Street Clinic, 175 Swan St. Free and part-pay; syphilis only.

Syphilis Clinic, Children's Hospital, 219 Bryant St. Free and part-pay; syphilis only.

Cambridge, Washington Co.: Mary McClellan Hospital. Free; all venereal diseases.

Camillus, Onondaga Co.: Camillus Clinic. Free; all venereal diseases.

Canastota, Madison Co.: Physician's Office, 129 Peterboro St. Free; all venereal diseases.

Cobleskill, Schoharie Co.: 4 Grand St. Free; all venereal diseases.

Coeymans, Albany Co.: Coeymans Clinic. Free and part-pay; all venereal diseases.

Cohoes, Albany Co.: Cohoes Venereal Clinic, City Hall. Free; all venereal diseases.

Corning, Steuben Co.: Corning City Clinic, City Hall. Free; all venereal diseases.

Cortland, Cortland Co.: Health Department, Courthouse. Free; all venereal diseases.

Dunkirk, Chautauqua Co.: Venereal Disease Clinic, Health Department, City Hall. Free; all venereal diseases.

East Kingston, Ulster Co.: East Kingston Clinic, Brigham St. Free; all venereal diseases.

East Rochester, Monroe Co.: East Rochester Venereal Disease Clinic, 113 West Ave. Free; all venereal diseases.

Elmira, Chemung Co.: City Dispensary, 425 East Market St. Free; all venereal diseases.

Elmont, Nassau Co.: V. D. Clinic, Department of Health, 765 Hempstead Turnpike. Free; all venereal diseases.

Endicott, Broome Co.: Village Clinic, 412 East Main St. Free; all venereal diseases.

Freeport, Nassau Co.: V. D. Clinic, Department of Health, Municipal Building, 46 North Ocean Ave. Free; all venereal diseases.

Fulton, Oswego Co.: 192 South First St. Free; all venereal diseases.

Geneva, Ontario Co.: Geneva City Clinic, Geneva General Hospital. Free; all venereal diseases.

Glen Cove, Nassau Co.: V. D. Clinic, Department of Health, 50 Glen St. Free; all venereal diseases.

Glens Falls, Warren Co.: Glens Falls Social Hygiene Clinic, 59 Ridge St. Free; all venereal diseases.

Gloversville, Fulton Co.: Health Department, 19 West Fulton St. Free; all venereal diseases.

Gouverneur, St. Lawrence Co.: Venereal Clinic, 25 John St. Free; all venereal diseases.

Greenburgh, Westchester Co.: Westchester Co. Department of Health, Tarrytown Road. Free; syphilis only.

Hornell, Steuben Co.: Steuben Co. Health Department, 108 Broadway. Free: all venereal diseases.

Hudson, Columbia Co.: Syphilis Clinic, 613 Warren St. Free; all venereal diseases.

Hudson Falls, Washington Co.: Washington Co. Syphilis Clinic, 235¼ Main St. Free; all venereal diseases.

Ithaca, Tompkins Co.:

Ithaca City Clinic, 115 North Tioga St. Free; all venereal diseases.

Tompkins Co. Clinic, Old Courthouse. Free; all venereal diseases.

Jamestown, Chautauqua Co.: Social Hygiene Clinic, 4 Forest Ave. Free; all venereal diseases.

Johnson City, Broome Co.:

Endicott Johnson Clinic, 65 Broad St. Free; all venereal diseases.

Dr. Walter J. Farrell's Office, 301 Main St. Part-pay; all venereal diseases.

Johnstown, Fulton Co.: Physician's Office, 9 South William St., Department of Public Health and Welfare. Free; all venereal diseases.

Kenmore, Erie Co.: Erie Co. Clinic, 2770 Delaware Ave. Free; syphilis only.

Kingston, Ulster Co.: Board of Health Clinic, 27 East O'Reilly St. Free; all venereal diseases.

Lackawanna, Erie Co.:

Friendship House, 195 Ridge Road. Free; all venereal diseases.

Lady of Victory, Ridge Road. Free; syphilis only.

Lawrence, Nassau Co.: V. D. Clinic, Department of Health. Free; all venereal diseases.

Little Falls, Herkimer Co.: V. D. Clinic, City Hall, Health Department. Free; syphilis only.

Lockport, Niagara Co.: Health Center, Fire Headquarters Building. Free; all venereal diseases.

Malone, Franklin Co.: Syphilis Clinic, Alice Hyde Hospital, Park St. Free; all venereal diseases.

Mamaroneck, Westchester Co.: Westchester Co. Department of Health, 234 Stanley Ave. Free; syphilis only.

Middletown, Orange Co.: Board of Health Clinic, City Hall. Free; all venereal diseases.

Mineola, Nassau Co.: V. D. Clinic, Department of Health, 68 Old Country Road. Free; all venereal diseases.

Monticello, Sullivan Co.: Monticello Clinic, Bushnell Building. Free; syphilis only.

Mount Vernon, Westchester Co.: Syphilis and Gonorrhea Clinic, Health Department, City Hall. Free; all venereal diseases except granuloma inguinale.

Newburgh, Orange Co.: Board of Health Clinic, 255 Broadway. Free; all venereal diseases.

New Rochelle, Westchester Co.: Department of Health, 30 Church St. Free; all venereal diseases.

New York City, Manhattan:

Beekman Street Hospital, 117 Beekman St., V. D. Clinic. Part-pay; all venereal diseases.

Bellevue Hospital, V. D. Clinic, First Ave. and 26th St. Free; all venereal diseases.

New York City, Manhattan—Continued.

Beth David Hospital, V. D. Clinic, 1720 Second Ave. Free and part-pay; all venereal diseases.

Beth Israel Hospital, 17 Stuyvesant Park East, V. D. Clinic. Free and part-pay; all venereal diseases.

Central Clinic, Department of Health V. D. Clinic, 125 Worth St. Free; all venereal diseases.

Central Harlem Clinic, Department of Health V. D. Clinic, 2238 Fifth Ave. Free; all venereal diseases.

City Hospital Dispensary, 535 East 80th St. Free; all venereal diseases.

Columbus Hospital, V. D. Clinic, 226 East 20th St. Free; and part-pay; all venereal diseases.

Community Hospital, V. D. Clinic, 8 St. Nicholas Place. Part-pay; all venereal diseases.

East Harlem Clinic, Department of Health V. D. Clinic, 158 East 115th St. Free; all venereal diseases.

Flower-Fifth Avenue Hospital, V. D. Clinic, 1 East 105th St. Part-pay; syphilis only.

French Hospital, V. D. Clinic, 324 West 30th St. Part-pay; all venereal diseases.

Good Samaritan Dispensary, V. D. Clinic, 75 Essex St. Part-pay; all venereal diseases.

Gouverneur Hospital, V. D. Clinic, Gouverneur Slip. Free; all venereal diseases.

Harlem Eye & Ear Hospital, V. D. Clinic, 127th St. and Lexington Ave. Free; syphilis only.

Harlem Hospital, 136th St. and Lenox Ave. Free; all venereal diseases.

Jewish Memorial Hospital, Broadway and 196th St. Part-pay; all venereal diseases.

Joint Diseases Hospital, 45 East 123rd St. Free and part-pay; all venereal diseases.

Knickerbocker Hospital, 70 Convent Ave. Part-pay; syphilis only.

Lenox Hill Hospital, Park Ave. and 76th St. Part-pay; all venereal diseases.

Lower West Side Clinic, Department of Health, 303 Ninth Ave. Free; all venereal diseases.

Lutheran Hospital, 144th St. and Convent Ave. Part-pay; all venereal diseases.

Manhattan Eye and Ear, 210 East 64th St. Part-pay; syphilis only.

Meinhard Clinic, Department of Health, 130 East 101st St. Free; all venereal diseases.

Metropolitan Dispensary, 535 East 80th St. Free; all venereal diseases.

Midtown Hospital, 309 East 49th St. Part-pay; all venereal diseases.

Misericordia Hospital, 531 East 86th St. Free; syphilis only.

Mount Sinai Hospital, 100th St. and Madison Ave. Free and part-pay; all venereal diseases.

New York Dispensary, 34 Spring St. Free and part-pay; all venereal diseases.

New York Eye and Ear, Second Ave. and 13th St. Part-pay; syphilis only.

New York Hospital, 525 East 68th St. Free and part-pay; all venereal diseases.

New York Infirmary, 321 East 15th St. Free and part-pay; all venereal diseases.

New York City, Manhattan—Continued.

New York Polyclinic Hospital, 341 West 50th St. Part-pay; all venereal diseases.

New York Skin and Cancer Unit of Post-Graduate Hospital, 301 East 19th St. Part-pay; syphilis only.

New York Post-Graduate Hospital, 303 East 20th St. Free and part-pay; gonorrhea only.

New York University, 463 First Ave. Part-pay; all venereal diseases.

Northeastern Dispensary, 222 East 59th St. Part-pay; all venereal diseases.

Northwestern Dispensary, 403 West 36th St. Part-pay; all venereal diseases.

Roosevelt Hospital, 59th St. and 9th Ave. Part-pay; all venereal diseases.

Ruptured and Crippled Hospital, 321 East 42d St. Part-pay; syphilis only.

St. Clare's Hospital, 415 West 51st St. Part-pay; all venereal diseases.

St. Luke's Hospital, Amsterdam Ave. and 113th St. Part-pay; all venerea. diseases.

St. Vincent's Hospital, 7th Ave. and 11th St. Free and part-pay; all venereal diseases.

St. Vincent's Clinic, Department of Health, 7th Ave. and 11th St. Free; all venereal diseases.

Stuyvesant Polyclinic Hospital, 137 Second Ave. Part-pay; all venereal diseases.

Sydenham Hospital, 565 Manhattan Ave. Part-pay; all venereal diseases.

Vanderbilt Clinic, Broadway and 167th St. Part-pay; syphilis only.

Washington Clinic, Department of Health, 128 Prince St. Free; all venereal diseases.

West Side Hospital, 446 West 43d St. Free and part-pay; all venereal diseases.

New York City, Bronx:

Bronx Hospital, 169th St. and Fulton Ave. Part-pay; all venereal diseases.

Fordham Hospital, Southern Blvd. and Crotona Ave. Free; all venereal diseases.

Lebanon Hospital, Westchester and Cauldwell Aves. Free and part-pay; all venereal diseases.

Lincoln Hospital, 141st St. and Concord Ave. Free; all venereal diseases.

Morrisania Hospital, 168th St. and Gerard Ave. Free; all venereal diseases.

Mott Haven Health Center, Department of Health, 349 East 140th St. Free; all venereal diseases.

Tremont Clinic, Department of Health, 1826 Arthur Ave. Free; all venereal diseases.

New York City, Brooklyn:

Beth Moses Hospital, 404 Hart St. Part-pay; all venereal diseases.

Brooklyn Hospital, De Kalb Ave. and Ashland Place. Part-pay; all venereal diseases.

Brooklyn Eye and Ear Hospital, 29 Greene Ave. Free and part-pay; syphilis only.

Bushwick Health Center, Department of Health, 186 Grove St. Free; all venereal diseases.

Cumberland Hospital, 39 Auburn Place. Free; syphilis only.

Greenpoint Hospital, Kingsland Ave. Free; all venereal diseases.

Harbor Hospital, Cropsey Ave. and Bay 32d St. Part-pay; all venereal diseases.

Israel Zion Hospital, 4802 Tenth Ave. Part-pay; syphilis only.

Jewish Hospital, 555 Prospect Place. Part-pay; all venereal diseases.

New York City, Brooklyn—Continued.

Kings County Hospital, 451 Clarkson Ave. Free; all venereal diseases.

Long Island College Hospital, Henry, Pacific, and Amity Sts. Part-pay; all venereal diseases.

Lutheran Hospital, East New York Ave. and Junius St. Part-pay; all venereal diseases.

Methodist Hospital, 6th St. and 7th Ave. Part-pay; gonorrhea only.

Ocean Hill Memorial Hospital, 343 Ralph Ave. Part-pay; all venereal diseases.

Red Hook-Gowanus Clinic, Department of Health, 250 Baltic St. Free; all venereal diseases.

St. John's Hospital, 480 Herkimer St. Free and part-pay; syphilis only.

Williamsburg-Greenpoint Clinic, Department of Health, 151 Maujer St. Free; all venereal diseases.

New York City, Queens:

Astoria-Long Island City Clinic, Department of Health, 12–26 31st Ave. Free; all venereal diseases.

Far Rockaway Clinic, Department of Health, 1517 Central Ave. Free; all venereal diseases.

Flushing Hospital, Parsons Boulevard. Part-pay; syphilis only.

Flushing-Corona Clinic, Department of Health, 34–33 Junction Blvd. Free; all venereal diseases.

Jamaica West Clinic, Department of Health, 92–18 149th St. Free; all venereal diseases.

Queens General Hospital, 161st St. and 82d Drive. Free; all venereal diseases.

St. John's Long Island City Hospital, Jackson Ave. and 12th St. Free and part-pay; all venereal diseases.

New York City, Richmond:

Old Court House Clinic, Department of Health, 302 Center Ave. Free; all venereal diseases.

Richmond Venereal Disease Clinic, Department of Health, 51 Stuyvesant Place. Free; all venereal diseases.

Niagara Falls, Niagara Co.: Syphilis Clinic, Bureau of Health, City Hall. Free; all venereal diseases.

North Tonawanda, Niagara Co.: Syphilis Clinic, Health Department, City Hall. Free; syphilis only.

Norwich, Chenango Co.: Chenango Memorial Hospital, 179 North Broad St. Free; syphilis only.

Ogdensburg, St. Lawrence Co.: V. D. Clinic, City Hall. Free; all venereal diseases.

Olean, Cattaraugus Co.: Olean Clinic, City Building. Free; all venereal diseases.

Oneida, Madison Co.: Oneida Clinic, Oneida City Hospital. Free; all venereal diseases.

Oneonta, Otsego Co.: Dr. E. J. Keegan's Office. Free; all venereal diseases.

Ossining, Westchester Co.: Ossining Hospital, Spring St. Free; syphilis only.

Oswego, Oswego Co.: V. D. Clinic, Health Center. Free; all venereal diseases.

Peekskill, Westchester Co.: Westchester Co. Department of Health, Municipal Building. Free; syphilis only.

Plattsburg, Clinton Co.: Venereal Disease Clinic, City Hall. Free; all venereal diseases.

Port Chester, Westchester Co.: Health Center, 350 North Main St. Free; all venereal diseases.

Port Jervis, Orange Co.: City Venereal Clinic Health Center, 21 Ulster Place. Free; all venereal diseases.

Poughkeepsie, Dutchess Co.:

Syphilis Control and Gonorrhea, Board of Health, 24 Washington St. Free; all venereal diseases.

Dutchess Co. Health Center, 14 Fairmont Ave. Free; all venereal diseases.

Rochester, Monroe Co.:

Baden St. Dispensary, 160 Baden St. Free and pay or part-pay; all venereal diseases.

Genesee Hospital, 224 Alexander St. Part-pay; syphilis only.

Highland Hospital, 3 Bellevue Drive. Free and pay or part-pay; syphilis only.

Rochester General Hospital, 501 Main St., West. Free; all venereal diseases.

St. Mary's Hospital, 909 West Main St. Free and pay; all venereal diseases.

Strong Memorial Hospital, 260 Crittenden Blvd. (Children only.) Part-pay; syphilis only.

Rome, Oneida Co.: Rome Syphilis Control Clinic, 119 East Dominick St. Free; all venereal diseases.

Salamanca, Cattaraugus Co.: Cattaraugus Co. Clinic, 27 Maple St. Free; all venereal diseases.

Saranac Lake, Franklin Co.: V. D. Clinic, Board of Health, Town Hall, Main St. Free; all venereal diseases.

Saratoga Springs, Saratoga Co.: Syphilis Clinic, Saratoga Hospital. Free; all venereal diseases.

Schenectady, Schenectady Co.: Schenectady Co. Public Health Committee, Syphilis Division, 508 Union St. Free; all venereal diseases.

Sodus, Wayne Co.: Dr. A. D. Ryan's Office, 81 Main St. Part-pay; all venereal diseases.

Syracuse, Onondaga Co.: Social Hygiene Clinic, Department of Health, 610 East Fayette St. Part-pay; all venereal diseases.

Tarrytown, Westchester Co.: Tarrytown Hospital. Free; syphilis only.

Tonawanda, Erie Co.: Tonawanda Clinic, 201 Fletcher St. Free; syphilis only.

Troy, Rensselaer Co.:

Municipal Clinic, Health Department. Free; all venereal diseases.

Troy Hospital, Oakwood Ave. Free and pay (if able); syphilis and gonorrhea only.

Tupper Lake, Franklin Co.: Mercy General Hospital, 114 Wanbeek Ave. Free; all venereal diseases.

Utica, Oneida Co.: Utica Dispensary, 406 Elizabeth St. Free and pay or part-pay; all venereal diseases.

Valhalla, Westchester Co.: Grasslands Hospital. Free; syphilis only.

Warsaw, Wyoming Co.: Wyoming Co. Community Hospital, 113 West Buffalo St. Free; all venereal diseases.

Watertown, Jefferson Co.: V. D. Clinic, 113 Park Place. Free; all venereal diseases.

Watkins Glen, Schuyler Co.: Schuyler Co. Venereal Disease Clinic, Health Center, Franklin St. Free; all venereal diseases.

Wellsville, Allegany Co.: Wellsville Clinic, 233 North Main St. Free; syphilis and gonorrhea.

Whitehall, Washington Co.: Syphilis Clinic, 1 North Main St. Free; all venereal diseases.

White Plains, Westchester Co.: Department of Health, 10 Depot Plaza. Free; syphilis only.

Yonkers, Westchester Co.: Social Hygiene Clinic, 90 Main St. Free; all venereal diseases.

NORTH CAROLINA

Addor, Moore Co.: Moore Co. Health Department, Clinic House. Free; all venereal diseases.

Ahoskie, Hertford Co.: Hertford Co. Health Department, Vann Warehouse Building. Free; all venereal diseases.

Albemarle, Stanly Co.: Stanly Co. Health Department, Library Bldg. Free; syphilis only.

Andrews, Cherokee Co.: Cherokee Co. Health Department. Free; syphilis and gonorrhea only.

Angier, Harnett Co.: Harnett Co. Health Department, Wilson Clinic Building. Free; all venereal diseases.

Ansonville, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Apex, Wake Co.: Wake Co. Health Department. Free; syphilis only.

Arden, Buncombe Co.: Buncombe Co. Health Department. Dr. Baker's Office. Free; syphilis and gonorrhea only.

Asheboro, Randolph Co.: Randolph Co. Health Department, Courthouse. Free; all venereal diseases.

Asheville, Buncombe Co.:

Buncombe Co. Health Department, Courthouse Jail. Free; syphilis and gonorrhea only.

City Health Department, Market Bldg. Free; all venereal diseases.

Ayden, Pitt Co.: Pitt Co. Health Department, Town Hall, Main St. Free; all venereal diseases.

Badin, Stanly Co.: Stanly Co. Health Department, Basement of Badin Hospital. Free; syphilis only.

Bailey, Nash Co.: Nash Co. Health Department, Bank Bldg. Free; syphilis only.

Battleboro, Nash Co.: Nash Co. Health Department. Dr. A. W. Deans' Office. Free; syphilis only.

Belhaven, Beaufort Co.: Beaufort Co. Health Department, Bank Bldg. Free and part-pay; all venereal diseases.

Belmont, Gaston Co.: Gaston Co. Health Department, Davis Bldg. Free; all venereal diseases.

Benson, Johnston Co.: Johnston Co. Health Department, Post Office. Free; all venereal diseases.

Bessemer City, Gaston Co.: Gaston Co. Health Department, over City Hall. Free; all venereal diseases.

Bethel, Pitt Co.: Pitt Co. Health Department, Main St. Free; all venereal diseases.

Beulaville, Duplin Co.: Duplin Co. Health Department Mobile Unit. Free; all venereal diseases.

Black Mountain, Buncombe Co.: Buncombe Co. Health Department, Howerton Bldg. Free; syphilis and gonorrhea only.

North Carolina

Boone, Watauga Co.: Watauga Co. Health Department, County Office Bldg. Free; all venereal diseases.

Boonville, Yadkin Co.: Yadkin Co. Health Department, Main St. Free; all venereal diseases.

Brevard, Transylvania Co.: Health Department, Tinsley Bldg. Free; syphilis only.

Bridgeton, Craven Co.: Craven Co. Health Department Mobile Unit. Free; syphilis only.

Bryson City, Swain Co.: Swain Co. Health Department, Courthouse. Free; syphilis and gonorrhea only.

Burlington, Alamance Co.: Alamance Co. Health Department, Fisher St. Free; syphilis only.

Burnsville, Yancey Co.: Health Department, Briggs Bldg. Free; syphilis and gonorrhea only.

Cairo, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Calypso, Duplin Co.: Duplin Co. Health Department Mobile Unit. Free; all venereal diseases.

Candler, Buncombe Co.: Buncombe Co. Health Department. Dr. Willis' Office. Free; syphilis and gonorrhea only.

Canton, Haywood Co.: Haywood Co. Health Department, Champion Laboratory Bldg., Main St. Free; syphilis only.

Carthage, Moore Co.: Moore Co. Health Department, Courthouse. Free; all venereal diseases.

Cason's Old Field, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Cedar Hill, Anson Co.: Anson Co. Health Department Mobile Unit, Highway 52 North. Free; all venereal diseases.

Chadbourn, Columbus Co.: Columbus Co. Health Department, Legion Hut. Free; all venereal diseases.

Chapel Hill, Orange Co.: Orange Co. Health Department Bldg. Free; syphilis and gonorrhea only.

Charlotte, Mecklenburg Co.:

City Health Department, 615 East 4th St. Free; all venereal diseases.

Mecklenburg Co. Health Department, Steele Creek Maternity Clinic, Route 3. Free; syphilis only.

Mecklenburg Co. Health Department, Mt. Holly Road, Route 6. Free; syphilis only.

Cherokee, Swain Co.: Cherokee Reservation Hospital. Free; all venereal diseases.

Cherryville, Gaston Co.: Gaston Co. Health Department, Over City Hall. Free; all venereal diseases.

China Grove, Rowan Co.: Rowan Co. Health Department. Free; syphilis only.

Chinquapin, Duplin Co.: Duplin Co. Health Department Mobile Unit. Free; all venereal diseases.

Clarkton, Bladen Co.: Bladen Co. Health Department, C. S. Clark Bldg. Free; syphilis only.

Cleveland, Rowan Co.: Rowan Co. Health Department, Main St. Free; syphilis only.

Cliffside, Rutherford Co.: Office of Drs. Moss and Jones. Free; syphilis only.

Clinton, Sampson Co.: Sampson Co. Health Department, Courthouse. Free; all venereal diseases.

Colerain, Bertie Co.: Bertie Co. Health Department, Bank Bldg., 2d Floor. Free; syphilis and gonorrhea only.

Columbia, Tyrrell Co.: Tyrrell Co. Health Department, Agricultural Bldg. Free; all venereal diseases.

Como, Hertford Co.: Hertford Co. Health Department, Town Hall, Main St. Free; all venereal diseases.

Concord, Cabarrus Co.: Cabarrus Co. Health Department, County Bldg., South Church St. Free; syphilis only.

Cooleemee, Davie Co.: Davie Co. Health Department, Episcopal Church. Free; all venereal diseases.

Cove City, Craven Co.: Craven Co. Health Department Mobile Unit. Free; syphilis only.

Coxe-Bennett, Anson Co.: Anson Co. Health Department Mobile Unit, Highway 52 North. Free; all venereal diseases.

Creedmoor, Granville Co.: Granville Co. Health Department. Dr. Joseph Thompson's Office, Main St. Free; all venereal diseases.

Creswell, Washington Co.: Washington Co. Health Department. Dr. J. M. Phelps' Office. Free; all venereal diseases.

Currituck, Currituck Co.: Currituck Co. Health Department Bldg. Free; all venereal diseases.

Davidson, Mecklenburg Co.: Mecklenburg Co. Health Department. Free; syphilis only.

Deep Creek, Anson Co.: Anson Co. Health Department Mobile Unit, Mr. G. K. Little's Store. Free; all venereal diseases.

Deep Run, Lenoir Co.: Lenoir Co. Health Department Mobile Unit. Free; syphilis only.

Dobson, Surry Co.:

Surry Co. Health Department, County Jail. Free; all venereal diseases.

Surry Co. Health Department, Prison Camp, Route 1. Free; syphilis only.

Dover, Craven Co.: Craven Co. Health Department Mobile Unit. Free; syphilis only.

Dunn, Harnett Co.: Harnett Co. Health Department, South Wilson Ave. Free; all venereal diseases.

Durham, Durham Co.:

Duke Hospital. (Children only.) Free; all venereal diseases.

Duke Hospital. Pay; all venereal diseases.

Health Department, Courthouse. Free; all venereal diseases.

Lincoln Hospital. (Negro only.) Pay; syphilis only.

Watts Hospital. Pay; all venereal diseases.

Edenton, Chowan Co.: Health Department Bank of Edenton Bldg. Free; syphilis and gonorrhea only.

Elizabeth City, Pasquotank Co.: City Health Department, Kramer Bldg. Free; all venereal diseases.

Elizabethtown, Bladen Co.: Bladen Co. Health Department. Free; syphilis only.

Elkin, Surry Co.: Surry Co. Health Department, City Hall. Free; all venereal diseases.

Ellerbe, Richmond Co.: Richmond Co. Health Department, City Hall. Free; syphilis only.

Elm City, Wilson Co.: Wilson Co. Health Department. Dr. R. H. Putney's Office. Free; syphills only.

Elm Grove, Lenoir Co.: Lenoir Co. Health Department Mobile Unit. Free; syphilis only.

Enfield, Halifax Co.: Halifax Co. Health Department, Whitehead Drugstore Bldg. Free; syphilis and gonorrhea only.

Englehard, Hyde Co.: Hyde Co. Health Department, Rufus Williams Store Bldg, 2d Floor. Free; all venereal diseases.

Fairmont, Robeson Co: Robeson Co. Health Department, Grantham Bldg., Main St. Free; syphilis and gonorrhea only.

Faison, Duplin Co.: Duplin Co. Health Department Mobile Unit. Free; all venereal diseases.

Falling Creek, Lenoir Co.: Lenoir Co. Health Department Mobile Unit. Free; syphilis only.

Farmville, Pitt Co.: Pitt Co. Health Department, McKinney's Hall, Main St. Free; all venereal diseases.

Fayetteville, Cumberland Co.: Cumberland Co. Health Department, Courthouse (Basement). Free; syphilis and gonorrhea only.

Forest City, Rutherford Co.: Rutherford Co. Health Department, City Hall. Free; syphilis only.

Fort Barnwell, Craven Co.: Craven Co. Health Department Mobile Unit. Free; syphilis only.

Franklin, Macon Co.: Health Department, Asher Bldg. Free; syphilis and gonorrhea only.

Fremont, Wayne Co.: Wayne Co. Health Department, City Hall. Free; syphilis, gonorrhea, and chancroid only.

Fuquay Springs, Wake Co.: Wake Co. Health Department, Elliott Bldg., Main St. Free; syphilis only.

Garland, Sampson Co.: Sampson Co. Health Department. Dr. Johnson's Office. Free; all venereal diseases.

Garris Grove, Anson Co.: Anson Co. Health Department Mobile Unit, Highway 109 North. Free; all venereal diseases.

Gaston, Northampton Co.: Northampton Co. Health Department, Post Office Bldg. Free; syphilis only.

Gastonia, Gaston Co.: Gaston Co. Health Department. Free; all venereal diseases.

Goldsboro, Wayne Co.:

Goldsboro Hospital. Free; syphilis, gonorrhea, and chancroid only.

Wayne Co. Health Department, Courthouse. Free; syphilis, gonorrhea, and chancroid only.

Gowers, Lenoir Co.: Lenoir Co. Health Department Mobile Unit. Free; syphilis only.

Graham, Alamance Co.: Alamance Co. Health Department, 3d Floor, Courthouse. Free; syphilis only.

Graingers, Lenoir Co.: Lenoir Co. Health Department Mobile Unit. Free; syphilis only.

Grandy, Currituck Co.: Currituck Co. Health Department, Woodhouse Bldg. Free; all venereal diseases.

Granite Falls, Caldwell Co.: Caldwell Co. Health Department, Parks Bldg. Free; all venereal diseases.

Green Hill, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Greensboro, Guilford Co.:
Guilford Co. Health Department, City Hall, Green and Gaston Sts. Free; all venereal diseases.
Guilford Co. Home. Free; all venereal diseases.
Terra Cotta Community Center House. Free; all venereal diseases.

Greenville, Pitt Co.: Pltt Co. Health Department, 2d Floor, County Bldg., Third St. Free; all venereal diseases.

Grifton, Craven Co.: Craven Co. Health Department Mobile Unit, Riverside Church, Route 1. Free; syphilis only.

Hamlet, Richmond Co.: Richmond Co. Health Department, City Hall. Free; syphilis only.

Hamlock, Craven Co.: Craven Co. Health Department Mobile Unit, Melvin Church. Free; syphilis only.

Hanes, Forsyth Co.: Forsyth Co. Health Department. Free; all venereal diseases.

Harrellsville, Hertford Co.: Hertford Co. Health Department. Free; all venereal diseases.

Hayesville, Clay Co.: Clay Co. Health Department. Free; syphilis and gonorrhea only.

Henderson, Vance Co.:
Vance Co. Health Department, Garnett St. Free; all venereal diseases.
Dr. Beckford's Office. Free; all venereal diseases.

Hickory, Catawba Co.: Catawba Co. Health Department, Clines Bldg. Free; syphilis and gonorrhea only.

High Point, Guilford Co.: City Health Department, 112½ North Wreen St. Free; syphilis only.

Hillsboro, Orange Co.: Orange Co. Health Department. Free; syphilis and gonorrhea only.

Hoffman, Richmond Co.: Richmond Co. Health Department, Colored Methodist Church. Free; syphilis only.

Hookerton, Greene Co.: Greene Co. Health Department, Drs. Dawson & Carroll's Office, Main St. Free; syphilis only.

Horne School (colored), Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Huntersville, Mecklenburg Co.: Mecklenburg Co. Health Department, Dr. T. Craven's Office. Free; syphilis and gonorrhea only.

Hugo, Lenoir Co.: Lenoir Co. Health Department Mobile Unit. Free; syphilis only.

Institute, Lenoir Co.: Lenoir Co. Health Department Mobile Unit. Free; syphilis only.

Jackson, Northampton Co.:
Northampton Co. Health Department. Free; syphilis only.
Northampton Co. Health Department, Ranson School, The Neck. Free; syphilis only.

Jefferson, Ashe Co.: Ashe Co. Health Department, Old McNell Store Bldg. Free; all venereal diseases.

Kannapolis, Cabarrus Co.: Cabarrus Co. Health Department, Main Street, over Belk's Store. Free; syphilis only.

Kenansville, Duplin Co.:
Duplin Co. Health Department. Free; all venereal diseases.
Duplin Co. Health Department Mobile Unit, B. F. Grady. Free; all venereal diseases.

Kenly, Johnston Co.: Johnston Co. Health Department, Dr. Woodward's Office. Free; all venereal diseases.

Kernersville, Forsyth Co.: Forsyth Co. Health Department. Free; all venereal diseases.

Kerr, Sampson Co.: Sampson Co. Health Department, Harrell's Store, Dr. Cox' Office. Free; all venereal diseases.

King, Stokes Co.: Stokes Co. Health Department, Beside Drugstore, Main St. Free; all venereal diseases.

Kings Mountain, Cleveland Co.: Cleveland Co. Health Department, City Hall (Basement). Free; all venereal diseases.

Kinston, Lenoir Co.:

Lenoir Co. Health Department, South Queen St. Free; syphilis only.

Lenoir Co. Health Department, Mobile Unit, Ed. Jones' Store. Free; syphilis only.

Lenoir Co. Health Department, Mobile Unit, W. H. Jones' Store. Free; syphilis only.

Lenoir Co. Health Department, Mobile Unit, Kilpatrick's Service Station. Free; syphilis only.

Lenoir Co. Health Department, Mobile Unit, Wootens' Cross Road. Free; syphilis only.

La Grange, Lenoir Co.: Lenoir Co. Health Department Mobile Unit. Free; syphilis only.

Lawndale, Cleveland Co.: Cleveland Co. Health Department. Free; all venereal diseases.

Leaksville, Rockingham Co.: Rockingham Co. Health Department. Free; all venereal diseases.

Lenoir, Caldwell Co.: Caldwell Co. Health Department, Courthouse. Free; all venereal diseases.

Lewiston-Kelford, Bertie Co.: Bertie Co. Health Department, Colored School. Free; syphilis and gonorrhea only.

Lexington, Davidson Co.: Davidson Co. Health Department, Varner Bldg., South Main St. Free; syphilis only.

Liberty, Randolph Co.: Randolph Co. Health Department, Smith Bldg. Free; all venereal diseases.

Lilesville, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Lillington, Harnet Co.: Harnet Co. Health Department, Front St., Agriculture Bldg. Free; all venereal diseases.

Lincolnton, Lincoln Co.: Lincoln Co. Health Department, County Courthouse. Free; syphilis and gonorrhea only.

Littleton, Halifax Co.: Halifax Co. Health Department, City Hall. Free; syphilis and gonorrhea only.

Long Pine, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Louisburg, Franklin Co.: Franklin Co. Health Department, North Main St. Free; syphilis and gonorrhea only.

Lumberton, Robeson Co.: Robeson Co. Health Department, Agricultural Bldg., 8th St. Free; syphilis and gonorrhea only.

Magnolia, Duplin Co.: Duplin Co. Health Department Mobile Unit. Free; all venereal diseases.

Manteo, Dare Co.: Dare Co. Health Department, Community Bldg. Free; all venereal diseases.

Marshville, Union Co.: Union Co. Health Department, Union Drug Co. Bldg. Free; all venereal diseases.

Matthews, Mecklenburg Co.: Mecklenburg Co. Health Department, Dr. T. N. Reid's Office. Free; syphilis only.

Maxton, Robeson Co.: Robeson Co. Health Department, Carpenter Bldg., Patterson St. Free; syphilis and gonorrhea only.

Mayodan, Rockingham Co.: Rockingham Co. Health Department, Over Sharon's Market. Free; all venereal diseases.

McFarland, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Mebane, Alamance Co.: Alamance Co. Health Department, Town Hall. Free; syphilis only.

Middlesex, Nash Co.: Nash Co. Health Department, Dr. E. C. Powell's Office. Free; syphilis only.

Mint Hill, Mecklenburg Co.: Mecklenburg Co. Health Department. Free; syphilis only.

Mocksville, Davie Co.: Davie Co. Health Department, Main St. Free; all venereal diseases.

Monroe, Union Co.: Union Co. Health Department, 210 West Franklin St. Free; all venereal diseases.

Morganton, Burke Co.: Burke Co. Health Department, Presnell Bldg. Free; all venereal diseases.

Morven, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Mt. Airy, Surry Co.: Surry Co. Health Department, City Hall. Free; all venereal diseases.

Mount Gilead, Richmond Co.: Richmond Co. Health Department, Community House, R. F. D. Free; syphilis only.

Mount Holly, Gaston Co.: Gaston Co. Health Department, over City Hall. Free; all venereal diseases.

Mount Olive, Wayne Co.: Wayne Co. Health Department, City Hall. Free; syphilis, gonorrhea, and chancroid only.

Mount Pleasant, Cabarrus Co.: Cabarrus Co. Health Department, Main St. Free; syphilis only.

Murfreesboro, Hertford Co.: Hertford Co. Health Department, Post Office Bldg., Main St. Free; all venereal diseases.

Murphy, Cherokee Co.: Cherokee Co. Health Department, Parker Bldg. Free; syphilis and gonorrhea only.

Nashville, Nash Co.: Nash Co. Health Department. Free; syphilis and gonorrhea only.

New Bern, Craven Co.:

Craven Co. Health Department, Courthouse, Broad St. Free; syphilis only.

Craven Co. Health Department, Good Shepherd Hospital, West St. Free; syphilis only.

Craven Co. Health Department Mobile Unit, Pine Grove Church, Route 4. Free; syphilis only.

Craven Health Department, Mobile Unit, Riverdale Church, Route 4. Free; syphilis only.

Newland, Avery Co.: City Health Department. Free; syphilis and gonorrhea only.

North Harlow, Craven Co.:
Craven Co. Health Department, Mobile Unit, Carter's Beer Garden. Free; syphilis only.
Craven Co. Health Department, Mobile Unit, Godette's Service Station. Free; syphilis only.

Newton, Catawba Co.: Catawba Co. Health Department, County Office Bldg. Free; syphilis and gonorrhea only.

Norwood, Stanly Co.: Stanly Co. Health Department, Barringer Bldg. Free; syphilis only.

Oxford, Granville Co.:
Granville Co. Health Department, Courthouse, Williamsboro St. Free; all venereal diseases.
Granville Co. Health Department, Peace's Store, Raleigh Rd. Free; all venereal diseases.

Peachland, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Pee Dee, Anson Co.: Anson Co. Health Department Mobile Unit, Frank Robinson's Store. Free; all venereal diseases.

Pembroke, Robeson Co.: Robeson Co. Health Department, Railroad St. Free; syphilis and gonorrhea only.

Pilot Mountain, Surry Co.: Surry Co. Health Department, Main St. Free; all venereal diseases.

Pinehurst, Moore Co.: Moore Co. Health Department, Fire House. Free; syphilis only.

Pinetops, Edgecombe Co.: Edgecombe Co. Health Department Mobile Unit, Store Bldg. Free; syphilis only.

Pineville, Anson Co.: Anson Co. Health Department. Free; syphilis only.

Piney Wood School (colored), Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Pink Hill, Lenoir Co.: Lenoir Co. Health Department Mobile Unit. Free; syphilis only.

Pittsboro, Chatham Co.: Chatham Co. Health Department, Health and Welfare Department Bldg. Free; syphilis and gonorrhea only.

Pleasant Hill, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Plymouth, Washington Co.: Washington Co. Health Department, Washington Co. Home. Free; all venereal diseases.

Polkton, Anson Co.: Anson Co. Health Department Mobile Unit, Railroad Station. Free; all venereal diseases.

Poplar Hill Church, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Raleigh, Wake Co.:
New Rex Hospital. Part-pay; syphilis and gonorrhea only.
Wake Co. Health Department, Old Rex Hospital Bldg., 17 West South St. Free; syphilis only.

Ramseur, Randolph Co.: Randolph Co. Health Department, Bank of Coleridge Bldg. Free; all venereal diseases.

Red Hill School (colored), Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Red Springs, Robeson Co.: Robeson Co. Health Department, Bank Bldg., Main St. Free; syphilis and gonorrhea only.

Reidsville, Rockingham Co.: Rockingham Co. Health Department, Community Bldg. Free; all venereal diseases.

Rich Square, Northampton Co.: Northampton Co. Health Department, Mattress Factory Bldg. Free; syphilis only.

Roanoke Rapids, Halifax Co.: Halifax Co. Health Department, Rosemary Clinic Bldg. Free; syphilis and gonorrhea only.

Robbinsville, Graham Co.: Graham Co. Health Department, Ingram's Bldg. Free; syphilis and gonorrhea only.

Robersonville, Martin Co.: Martin Co. Health Department, Main St. Free; all venereal diseases.

Rockingham, Richmond Co.: Richmond Co. Health Department, Courthouse. Free; syphilis only.

Rocky Ford Church, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Rocky Mount, Edgecombe Co.:

City Health Department, Municipal Bldg., 131½ North Main St. Free; all venereal diseases.

Edgecombe Co. Health Department Mobile Unit, Mt. Herman Church. Free; all venereal diseases.

Roseboro, Sampson Co.: Sampson Co. Health Department, Harris Bldg., Roseboro St. Free; all venereal diseases.

Rosehill, Duplin Co.: Duplin Co. Health Department Mobile Unit. Free; all venereal diseases.

Rowland, Robeson Co.: Robeson Co. Health Department, Main St. Free; syphilis and gonorrhea only.

Roxboro, Person Co.: Person Co. Health Department. Free; syphilis and gonorrhea only.

Rural Hall, Forsyth Co.: Forsyth Co. Health Department, Dr. Flynt's former Office Bldg. Free; all venereal diseases.

Rutherford College, Burke Co.: Burke Co. Health Department, Rutherford College Hospital. Free; all venereal diseases.

Rutherfordton, Rutherford Co.: Rutherford Co. Health Department, Courthouse. Free; all venereal diseases.

St. Pauls, Robeson Co.: Robeson Co. Health Department, Bank Bldg., Broad St. Free; syphilis and gonorrhea only.

Salisbury, Rowan Co.: Rowan Co. Health Department, Courthouse. Free; syphilis only.

Sanford, Lee Co.: Lee Co. Hospital. Free; syphilis only.

Scotland Neck, Halifax Co.: Halifax Co. Health Department. Free; syphilis and gonorrhea only.

Seaboard, Northampton Co.: Northampton Co. Health Department. Free; syphilis only.

Severn, Northampton Co.: Northampton Co. Health Department, White's Store Bldg. Free; syphilis only.

Shelby, Cleveland Co.: Cleveland Co. Health Department, Wethers-Blanton Bldg., Washington St. Free; all venereal diseases.

Siler City, Chatham Co.: Chatham Co. Health Department, Municipal Bldg. Free; syphilis and gonorrhea only.

Smithfield, Johnston Co.:

Johnston Co. Health Department, Courthouse. Free; all venereal diseases.

Johnston Co. Health Department, Opportunity Hall. Free; all venereal diseases.

Snow Hill, Greene Co.: Greene Co. Health Department, Agricultural Bldg. Free; syphilis only.

Sparta, Alleghany Co.: Alleghany Co. Health Department, County Courthouse. Free; all venereal diseases.

Speed, Edgecombe Co.: Edgecombe Co. Health Department, Mobile Unit, Railroad Station. Free; syphilis only.

Spring Hope, Nash Co.: Nash Co. Health Department, Mayor's Office. Free; syphilis only.

Stanley, Gaston Co.: Gaston Co. Health Department, Former Office of Dr. Taylor. Free; all venereal diseases.

Stantonsburg, Wilson Co.: Wilson Co. Health Department, Dr. D. B. Darden's Office. Free; syphilis only.

Statesville, Iredell Co.: Iredell Co. Health Department, Stearns Bldg. Free; all venereal diseases.

Stovall, Granville Co.: Granville Co. Health Department, Dr. Bradsher's Office. Free; all venereal diseases.

Swan Quarter, Hyde Co.: Hyde Co. Health Department, Agricultural Bldg. Free; all venereal diseases.

Sylva, Jackson Co.: Jackson Co. Health Department, Co. Courthouse. Free; syphilis only.

Tarboro, Edgecombe Co.:

Edgecombe Co. Health Department, Courthouse. Free; syphilis only.

Edgecombe Health Department, Mobile Unit, Store Bldg., Route 2. Free; syphilis only.

Thomasville, Davidson Co.: Davidson Co. Health Department, City Municipal Bldg., Guilford St. Free; syphilis only.

Tillery, Halifax Co.: Halifax Co. Health Department, Community Center. Free; syphilis and gonorrhea only.

Traphill, Wilkes Co.: Wilkes Co. Health Department, Masonic Bldg. Free; syphilis only.

Troy, Montgomery Co.: Montgomery Co. Health Department, Bank Bldg., Main St. Free; syphilis only.

Tryon, Polk Co.: St. Luke's Hospital. Free; all venereal diseases.

Vanceboro, Craven Co.: Craven Co. Health Department Mobile Unit. Free; syphilis only.

Wadesboro, Anson Co.: Anson Co. Health Department Mobile Unit, Agricultural Bldg., North Green St. Free; all venereal diseases.

Wake Forest, Wake Co.: Wake Co. Health Department, Wilkinson Bldg. Free; syphilis only.

Wallace, Duplin Co.: Duplin Co. Health Department Mobile Unit. Free; all venereal diseases.

Walnut Cover, Stokes Co.: Stokes Co. Health Department, Main St. Free; all venereal diseases.

Walstonburg, Greene Co.: Greene Co. Health Department, Dr. W. A. Marlowe's Office, Main St. Free; syphilis only.

Warsaw, Duplin Co.: Duplin Co. Health Department Mobile Unit. Free; all venereal diseases.

Washington, Beaufort Co.: Beaufort Co. Health Department, Agricultural Bldg. Free; all venereal diseases.

Waxhaw, Union Co.: Union Co. Health Department, Gamble Drug Co. Bldg. Free; all venereal diseases.

Waynesville, Haywood Co.: Haywood Co. Health Department, Courthouse, Main St. Free; syphilis only.

Weaverville, Buncombe Co.: Buncombe Co. Health Department, Dr. Sprinkle's Office. Free; syphilis and gonorrhea only.

Weldon, Halifax Co.: Halifax Co. Health Department. Free; syphilis and gonorrhea only.

Wendell, Wake Co.: Wake Co. Health Department, Underhill Bldg. Free; syphilis and gonorrhea only.

West Southern Pines, Moore Co.: Moore Co. Health Department. Free; all venereal diseases.

Whitakers, Edgecombe Co.: Edgecombe Co. Health Department, Doctor's Office. Free; syphilis only.

White Store, Anson Co.: Anson Co. Health Department Mobile Unit. Free; all venereal diseases.

Whiteville, Columbus Co.: Columbus Co. Health Department, Courthouse. Free; all venereal diseases.

Wilkesboro, Wilkes Co.: Wilkes Co. Health Department, Courthouse. Free; syphilis only.

Williamston, Martin Co.: Martin Co. Health Department, City Hall, Main St. Free; all venereal diseases.

Wilmington, New Hanover Co.: New Hanover Co. Health Department, Courthouse, 3d and Princess Sts. Free; all venereal diseases.

Wilson, Wilson Co.:

Mercy Hospital, East Green St. Free; syphilis only.

Wilson Co. Health Department, Courthouse, East Nash St. Free; syphilis only.

Windsor, Bertie Co.: Bertie Co. Health Department. Free; syphilis and gonorrhea only.

Winston-Salem, Forsyth Co.:

Forsyth Co. Health Department, 507 North West Blvd. Free; all venereal diseases.

Forsyth Co. Health Department, Health Center, Seventh and Highland Sts. Free; all venereal diseases.

Forsyth Co. Health Department, Ogburntown Health Center, Styers Bldg., Route 3. Free; all venereal diseases.

Winton, Hertford Co.: Hertford Co. Health Department. Free; all venereal diseases.

Yadkinville, Yadkin Co.: Yadkin Co. Health Department, Courthouse. Free; all venereal diseases.

Zebulon, Wake Co.: Wake Co. Health Department, Privett Bldg. Free; syphilis and gonorrhea only.

NORTH DAKOTA

Grand Forks, Grand Forks Co.: County Welfare Board Clinic. Free; all venereal diseases.

NOTE.—The venereal disease control program of North Dakota is based on a plan of payments made to private physicians for the treatment of venereal diseases in indigent patients. While only one clinic is functioning, the addresses of physicians giving treatment for venereal diseases under the State plan may be obtained from State, county, and municipal health officers.

OHIO

Addyston, Hamilton Co.: Hamilton Co. Health Department. Free; all venereal diseases.

Akron, Summit Co.:

Childrens Hospital, 182–200 West Bowery St. (Children under 15 years only.) Free; all venereal diseases.

City Hospital, 525 East Market St. (Children over 15 years only.) Free; all venereal diseases.

Detention Home, 2685 Mogadore Road. (Adults only.) Free; all venereal diseases.

Just-A-Mere Home and Hospital, 15 Broad St. Pay; all venereal diseases.

Munieipal Clinie, 11½ East Exchange St. (Adults and children over 15 years.) Free and part-pay; all venereal diseases.

Alliance, Stark Co.: Alliance Clinie. Part-pay; syphilis and gonorrhea only.

Bellaire, Belmont Co.: Venereal Treatments by Health Commissioner, Dankworth Building. Free and part-pay; all venereal diseases.

Bellefontaine, Logan Co.: County Health Board, 133 East Columbus St. Free; syphilis only.

Canton, Stark Co.: Canton Clinic, Auditorium Building. Free and part-pay; all venereal diseases.

Chillicothe, Ross Co.:

Board of Health Clinie, 65 East Second St. Part-pay; all venereal diseases.

Public Clinie, 65 East Main St. Pay; all venereal diseases.

Cincinnati, Hamilton Co.:

Babies' Fund Clinie, 1029 Findlay St. (Children only.) Free; syphilis only.

Babies' Fund Clinic, 1041 Cutter St. (Children only.) Free; syphilis only.

Babies' Fund Clinie, 320 Woodward St. (Children only.) Free; syphilis only.

Beckman Dispensary, 3212 Burnet Ave. (White only.) Free and part-pay; all venereal diseases.

Children's Hospital, Elland and Bethesda Aves. (Children only.) Free; syphilis only.

City Workhouse, 3208 Colerain Ave. Free; all venereal diseases.

General Hospital, Burnet Ave. and Goodman St. Free and part-pay; all venereal diseases.

General Hospital Pediatrie Venereal Clinie, Burnet Ave. (Children only.) Free and part-pay; syphilis and gonorrhea only.

Hamilton Co. Health Department, Steele Subdivision. Free; all venereal diseases.

Hamilton Co. Health Department, St. Simon, Woodlawn. Free; all venereal diseases.

Hamilton Co. Home & Chronie Disease Hospital, Hartwell. (Adults only.) Free; syphilis only.

Hamilton County Tuberculosis Sanitorium, Guerley Road. Free; syphilis only.

Health Center, 212 West 12th St. Free; all venereal diseases.

Health Department Clinie, 503 East Third St. (Adults only.) Free; all venereal diseases.

Mt. St. Mary's Training Sehool for Girls, Warsaw and Grand Aves. (White children only.) Free; all venereal diseases.

Cincinnati, Hamilton Co.—Continued.

Shoemaker Clinic, 1041 Cutter St. Part-pay; all venereal diseases.

Union Bethel Clinic, 501 East Third St. Part-pay; all venereal diseases.

Cleveland, Cuyahoga Co.:

City Hospital In-patient Department, 3395 Scranton Road. Free and pay or part-pay; all venereal diseases.

City Hospital Out-patient Department, 3395 Scranton Road. Free and part-pay; all venereal diseases.

Convent of Good Shepherd, East 30th St. and Carnegie Ave. (White and female only.) Free; all venereal diseases.

County Jail Hospital, Criminal Court Building, East 21st St. and Payne Ave. (Adults and children 16 years and up.) Free; all venereal diseases.

Division of Health Diagnostic Clinic, Room 22, City Hall. Free; all venereal diseases.

East 35th Street Dispensary of Cleveland City Hospital, 2500 East 35th St. (Children only.) Free and part-pay; all venereal diseases.

Fairview Park Hospital, 3305 Franklin Blvd. Free and part-pay; all venereal diseases.

Mt. Sinai Hospital, 1800 East 105th St. (Gonorrhea; female only.) Free and part-pay; all venereal diseases.

St. Alexis Hospital Dispensary, Broadway and McBride Ave. Free and part-pay; syphilis only.

St. Luke's Hospital, 11311 Shaker Blvd. Free and part-pay; all venereal diseases.

St. Vincent's Charity Hospital, East 22d St. at Central Ave. Free and pay or part-pay; all venereal diseases.

University Hospitals Babies and Children's Clinic, Adelbert Road. (Children only.) Free and part-pay; syphilis only.

University Hospitals Out-patient Department, 2065 Adelbert Road. Free and pay or part-pay; all venereal diseases.

Columbus, Franklin Co.:

Children's Hospital, 17th and Stone Sts. (Children only.) Free and part-pay; all venereal diseases.

Good Shepherd Convent, 63 South Sandusky St. (White children only.) Free; all venereal diseases.

Mt. Vernon Avenue Public Health Clinic, 980 Mt. Vernon Ave. Free; all venereal diseases.

State Bureau of Charities, 451 Oak St. (Children only.) Free; all venereal diseases.

State Institution for Blind. (Children only.) Free; all venereal diseases.

University Hospital, Ohio State University. (Adults only.) Part-pay; all venereal diseases.

White Cross Clinic, White Cross Hospital. (Adults only.) Part-pay; syphilis only.

Dayton, Montgomery Co.: Public Health Clinic, 334 Norwood Ave. Free and pay or part-pay; all venereal diseases.

East Cleveland, Cuyahoga Co.: Huron Road Hospital, 13951 Terrace Road. Free and part-pay; all venereal diseases.

East Liverpool, Columbiana Co.: City Health Clinic, City Hall, West 6th St. Free; all venereal diseases.

Hamilton, Butler Co.: Mercy Hospital Venereal Disease Clinic. Free; all venereal diseases.

Ironton, Lawrence Co.: Venereal Disease Clinic, City Bldg. Free; all venereal diseases.

Lakewood, Cuyahoga Co.: Lakewood Division of Health, 14517 Detroit Ave. Free, and pay or part-pay; all venereal diseases.

Lancaster, Fairfield Co.: Fairfield Co. Clinic, Courthouse. (Adults only.) Free; syphilis only.

Lima, Allen Co.: Memorial Venereal Clinic, Memorial Hospital, Linden and Mobile Aves. Free; all venereal diseases.

Logan, Hocking Co.: Hocking Co. Clinic. Free; syphilis only.

McArthur, Vinton Co.: Vinton Co. Clinic. Free; syphilis only.

Mansfield, Richland Co.: Mansfield Venereal Disease Clinic, City Building. Free; syphilis only.

Marion, Marion Co.: Marion Clinic, Delaware Ave. Free; all venereal diseases.

Middletown, Butler Co.: Venereal Disease Clinic, 101 North Broad St. Free; syphilis only.

Norwalk, Huron Co.: Huron Co. Health Department Clinic, Courthouse. Free; all venereal diseases.

Oxford, Butler Co.: Oxford Community, Municipal Building. Free; all venereal diseases.

Pomeroy, Meigs Co.: Meigs Co. Health Department, 116½ East Main St. Free; all venereal diseases.

Port Clinton, Ottawa Co.: The Pool Hospital, 125 East Third St. Part-pay; all venereal diseases.

Portsmouth, Scioto Co.: Health Center Clinic, 501 Court St. Free; syphilis only.

St. Clairsville, Belmont Co.: Belmont Co. Clinic. Free; all venereal diseases.

Sandusky, Erie Co.: Sandusky Venereal Disease Clinic, City Building. Free; all venereal diseases.

Sidney, Shelby Co.: Health Department, Courthouse. Free; all venereal diseases.

Springfield, Clark Co.: Municipal Hospital, East High St. Free; all venereal diseases.

Toledo, Lucas Co.:

Public Health Clinic, 9 Ontario St. Free; all venereal diseases.

St. Vincent's Dispensary, 2213 Cherry St. Free; syphilis only.

Troy, Miami Co.: Health Department Clinic, 119 West Main St. Free; all venereal diseases.

Warren, Trumbull Co.:

Public Health Clinic, 238 North Park Ave. Free; all venereal diseases.

Trumbull Co. Clinic, 303 Mahoning Ave. Free; all venereal diseases.

Warrensville, Cuyahoga Co.: Warrensville Correction Farm, Cooley Farms. (Adults only.) Free; all venereal diseases.

Waverly, Pike Co.: Pike Co. Board of Health. Free; syphilis only.

Xenia, Greene Co.: Greene Co. Health Department Public Health Clinic, City Bldg. Free; all venereal diseases.

Youngstown, Mahoning Co.: Venereal Disease Clinic, East Indianola Ave. Free and part-pay; all venereal diseases.

Zanesville, Muskingum Co.: City Clinic, Market House. Free and part-pay; all venereal diseases.

OKLAHOMA

Ada, Pontotoc Co.: City-County Health Department Clinic, Norris-Haney Bldg. Free; all venereal diseases.

Anadarko, Caddo Co.: County Health Department Clinic, 325 West Broadway. Free; all venereal diseases.

Antlers, Pushmataha Co.: County Health Department Clinic, Woodruff-Jones Bldg. Free; all venereal diseases.

Ardmore, Carter Co.: County Health Department Clinic, Fairgrounds. Free; all venereal diseases.

Arnett, Ellis Co.: County Health Department Clinic. Free; all venereal diseases.

Atoka, Atoka Co.: County Health Department Clinic, 207 West Court St. Free; all venereal diseases.

Beaver, Beaver Co.: County Health Department Clinic, Courthouse Basement. Free; all venereal diseases.

Boise City, Cimarron Co.: County Health Department Clinic, Courthouse, 2d Floor. Free; all venereal diseases.

Boynton, Muskogee Co.: County Health Department Clinic, Boynton Hotel. Free; all venereal diseases.

Bristow, Creek Co.: County Health Department Clinic, 300½ North Main St. Free; all venereal diseases.

Broken Bow, McCurtain Co.: County Health Department Clinic, Dr. Sizemore's Office. Free; all venereal diseases.

Carnegie, Caddo Co.: County Health Department Clinic. Free; all venereal diseases.

Cheyenne, Roger Mills Co.: County Health Department Clinic. Free; all venereal diseases.

Claremore, Rogers Co.: Venereal Disease Clinic, Courthouse Basement. Free; all venereal diseases.

Coalgate, Coal Co.: County Health Department Clinic, City Hall. Free; all venereal diseases.

Crescent, Logan Co.: County Health Department Clinic, over Good's Drug Store. Free; all venereal diseases.

Cushing, Payne Co.: County Health Department Clinic, 107½ East Moses St. Free; all venereal diseases.

Drumright, Creek Co.: County Health Department Clinic, 100½ East Broadway. Free; all venereal diseases.

Duncan, Stephens Co.: Venereal Disease Clinic, Courthouse. Free; all venereal diseases.

Durant, Bryan Co.: County Health Department Clinic, Brown Bldg. Free; all venereal diseases.

Enid, Garfield Co.: Venereal Disease Clinic, Courthouse. Free; all venereal diseases.

Guthrie, Logan Co.: County Health Department Clinic, 110½ West Oklahoma St. Free; all venereal diseases.

Guymon, Texas Co.: County Health Department Clinic, 105½ West 5th St. Free; all venereal diseases.

Hennessey, Kingfisher Co.: County Health Department Clinic, Memorial Hall. Free; all venereal diseases.

Henryetta, Okmulgee Co.: Venereal Disease Clinic, City Hall. Free; all venereal diseases.

Hugo, Choctaw Co.: County Health Department Clinic, City Hall. Free; all venereal diseases.

Idabel, McCurtain Co.: County Health Department Clinic, Courthouse. Free; all venereal diseases.

Jay, Delaware Co.: County Health Department Clinic, Public Health Bldg. Free; all venereal diseases.

Kingfisher, Kingfisher Co.: County Health Department Clinic, 119 South Main St. Free; all venereal diseases.

Konowa, Seminole Co.: County Health Department Clinic, Second Floor County Barn. Free; all venereal diseases.

Langston, Logan Co.: County Health Department Clinic, University Building. Free; all venereal diseases.

Lawton, Comanche Co.: County Health Department Clinic, 422½ "D" Ave. Free; all venereal diseases.

McAlester, Pittsburg Co.: Venereal Disease Clinic, Courthouse. Free; all venereal diseases.

Madill, Marshall Co.: County Health Department Clinic, W. P. A. Building. Free; all venereal diseases.

Marietta, Love Co.: County Health Department Clinic, Over Kelly Drug Store. Free; all venereal diseases.

Muskogee, Muskogee Co.: County Health Department Clinic, City Hall. Free; all venereal diseases.

Norman, Cleveland Co.: County Health Department Clinic, 601 East Gray St. Free; all venereal diseases.

Nowata, Nowata Co.: Venereal Disease Clinic, Commerce Exchange Bldg. Free; all venereal diseases.

Oklahoma City, Oklahoma Co.: County Health Department Clinic, 9 Wall St. Free; all venereal diseases.

Okmulgee, Okmulgee Co.: Venereal Disease Clinic, Colored Hospital. (Negro only.) Free; all venereal diseases.

Pauls Valley, Garvin Co.: County Health Department Clinic, Over Worley's Cafe. Free; all venereal diseases.

Picher, Ottawa Co.: Venereal Disease Clinic, 105 North Main St. Free; all venereal diseases.

Porter, Wagoner Co.: Venereal Disease Clinic, County Building. Free; all venereal diseases.

Poteau, Leflore Co.: County Health Department Clinic, Courthouse. Free; all venereal diseases.

Pryor, Mayes Co.: County Health Department Clinic, Health Center. Free; all venereal diseases.

Purcell, McClain Co.: County Health Department Clinic, Community Hall. Free; all venereal diseases.

Sallisaw, Sequoyah Co.: County Health Department Clinic, Over State Bank. Free; all venereal diseases.

Sapulpa, Creek Co.: County Health Department Clinic, Park and Dewey Sts. Free; all venereal diseases.

Seminole, Seminole Co.: County Health Department Clinic, Market Square Bldg. Free; all venereal diseases.

Shawnee, Pottawatomie Co.: County Health Department Clinic, 15 West 10th St. Free; all venereal diseases.

Stigler, Haskell Co.: Venereal Disease Clinic, Over Clout's Store. Free; all venereal diseases.

Stillwater, Payne Co.: County Health Department Clinic, 423 Main St. Free; all venereal diseases.

Stilwell, Adair Co.: County Health Department Clinic, Over Eagle Theater. Free; all venereal diseases.

Tahlequah, Cherokee Co.: County Health Department Clinic, Highway 62, 1½ miles east of Tahlequah. Free; all venereal diseases.

Tishomingo, Johnston Co.: County Health Department Clinic, W. P. A. Office. Free; all venereal diseases.

Tulsa, Tulsa Co.: City-County Health Department Clinic, 521 North Boulder St. Free; all venereal diseases.

Wagoner, Wagoner Co.: Venereal Disease Clinic, Above Wagoner Mercantile. Free; all venereal diseases.

Wewoka, Seminole Co.: County Health Department Clinic, City Hall. Free; all venereal diseases.

Woodward, Woodward Co.: County Health Department Clinic, City Hall. Free; all venereal diseases.

OREGON

Astoria, Clapsop Co.: Clapsop Co. Health Department, Flavel Memorial House. Free; all venereal diseases.

Baker, Baker Co.: Baker Co. Health Department, County Courthouse. Free; all venereal diseases.

Coquille, Coos Co.: Coos Co. Health Department, Courthouse. Free and part-pay; all venereal diseases.

Eugene, Lane Co.: Lane Co. Health Department, Courthouse. Free; all venereal diseases.

Grande Ronde, Polk Co.: Indian Service. Free; syphilis only.

Grants Pass, Josephine Co.: Josephine Co. Clinic, Courthouse. Free; all venereal diseases.

Hillsboro, Washington Co.: Washington Co. Health Department, County Courthouse. Free; all venereal diseases.

Klamath Agency, Klamath Co.: Klamath Co. Health Department. Free; all venereal diseases.

Klamath Falls, Klamath Co.: Klamath Co. Health Department, 8th and Pine Sts. Free; all venereal diseases.

La Grande, Union Co.: Union Co. Clinic. Free; all venereal diseases.

McMinnville, Yamhill Co.: Yamhill Co. Health Clinic, 333 North Davis St. Free; all venereal diseases.

Marshfield, Coos Co.: Coos Co. Health Department. Free and part-pay; all venereal diseases.

Medford, Jackson Co.: Jackson Co. Health Department, County Courthouse. Free; all venereal diseases.

Oregon City, Clackamas Co.: Clackamas Co. Health Department, 304 Courthouse. Part-pay; all venereal diseases.

Pendleton, Umatilla Co.: Umatilla Co. Health Unit, City Hall. Free; all venereal diseases.

Portland, Multnomah Co.: University of Oregon Medical School Clinic, 3181 S. W. Marquam Hill Road. Free (to those unable to pay); all venereal diseases.

Roseburg, Douglas Co.: Douglas Co. Health Department, Courthouse. Free; all venereal diseases.

Salem, Marion Co.: Marion Co. Department of Health, 495 State St. (Masonic Building.) Part-pay; all venereal diseases.

Siletz, Lincoln Co.: Indian Service. Free; syphilis only.

The Dalles, Wasco Co.: Wasco Co. Health Unit, Courthouse. Free; all venereal diseases.

PENNSYLVANIA

Abington, Montgomery Co.: Abington Memorial Hospital. Free, and pay or part-pay; all venereal diseases.

Allentown, Lehigh Co.:

Allentown Hospital Antiluetic Clinic. Free; syphilis only.

Sacred Heart Hospital, Chew St. Part-pay; all venereal diseases.

Altoona, Blair Co.: Altoona Hospital. Free; all venereal diseases.

Ashland, Schuylkill Co.: Ashland State Hospital. Free and part-pay; syphilis only.

Beaver Falls, Beaver Co.: Providence Hospital, Third Ave. Free; all venereal diseases.

Bedford, Bedford Co.: Pennsylvania Department of Health, Brode Building. Free; all venereal diseases.

Bellefonte, Centre Co.: White Building, Spring and High Sts. Free; syphilis only.

Bethlehem, Lehigh Co.: St. Luke's Hospital. Free and pay or part-pay; all venereal diseases.

Blairsville, Indiana Co.: Blairsville Clinic, 195 North Walnut St. Free; all venereal diseases.

Bloomsburg, Columbia Co.: Bloomsburg Hospital. Free; syphilis only.

Blossburg, Tioga Co.: Blossburg State Hospital. Free and pay; all venereal diseases.

Bradford, McKean Co.: Bradford Hospital. Free; all venereal diseases.

Bristol, Bucks Co.:

Dr. Wagner's Private Hospital, 435 Radcliffe St. Pay; syphilis only.

Venereal Control Clinic, Community House. Free; all venereal diseases.

Brownsville, Fayette Co.: Brownsville Hospital. Free; all venereal diseases.

Bryn Mawr, Montgomery Co.: Bryn Mawr Hospital. Part-pay; syphilis only.

Butler, Butler Co.: Butler Memorial Hospital. Free; all venereal diseases.

Carbondale, Lackawanna Co.: Genito-infectious Diseases Clinic, St. Joseph's Hospital. Free; all venereal diseases.

Carlisle, Cumberland Co.: Carlisle Hospital. Free; all venereal diseases.

Chambersburg, Franklin Co.: Chambersburg Hospital. Free; all venereal diseases.

Chester, Delaware Co.:

Chester Hospital, 9th and Barclay Sts. Free and part-pay; all venereal diseases.

Chester State Clinic, 400 East 8th St. Free; syphilis only.

Clarks Summit, Lackawanna Co.: Hillside Hospital for Mental Diseases. Free; neurosyphilis only.

Clearfield, Clearfield Co.: Clearfield Hospital. Free; all venereal diseases.

Coaldale, Schuylkill Co.: Coaldale State Hospital. Free; syphilis only.

Coatesville, Chester Co.: State Venereal Clinic, 260 East Main St. Free; syphilis only.

Columbia, Lancaster Co.: Columbia Hospital. Free; all venereal diseases.

Corry, Erie Co.: Corry Clinic, Municipal Building. Free; all venereal diseases.

Danville, Montour Co.: Geisinger Memorial Hospital. Pay and part-pay; syphilis only.

Darby, Delaware Co.: Fitzgerald-Mercy Hospital, Lansdowne Ave. and Bailey Road. Part-pay; all venereal diseases.

Drexel Hill, Delaware Co.: Delaware Co. Hospital, Lansdowne Ave. Free; all venereal diseases.

DuBois, Clearfield Co.: Genito-urinary Clinic, 2 South Main St. Free; all venereal diseases.

Easton, Northampton Co.: Easton Hospital. Free; all venereal diseases.

Erie, Erie Co.: State Clinic, 2117 Peach St. Free; all venereal diseases.

Farrell, Mercer Co.: State Clinic, First National Bank Building. Free; all venereal diseases.

Fountain Springs, Schuylkill Co.: Fountain Springs State Hospital. Free and part-pay; syphilis only.

Franklin, Venango Co.: Franklin Hospital Dispensary. Free; all venereal diseases.

Gettysburg, Adams Co.: Annie M. Warner Hospital. Free; syphilis only.

Greensburg, Westmoreland Co.: Westmoreland Hospital Association. Free; all venereal diseases.

Harrisburg, Dauphin Co.:

Harrisburg Clinic, 1114 North 6th St. Free; syphilis and gonorrhea only.

Harrisburg Hospital. Free and part-pay; all venereal diseases.

Polyclinic Hospital, Third and Radnor Sts. Free; all venereal diseases.

Hazleton, Luzerne Co.: City Hall. Free; syphilis only.

Homestead, Allegheny Co.: Syphilis Clinic, 301 East 8th Ave. Free; syphilis only.

Huntingdon, Huntingdon Co.: State Clinic, 821 Mifflin St. Free; all venereal diseases.

Indiana, Indiana Co.: State Clinic, Room H, Courthouse. Free; all venereal diseases.

Johnstown, Cambria Co.:

Lee Hospital, 320 Main St. Free; all venereal diseases.

State Clinic, 344 Lincoln St. Free; all venereal diseases.

Kane, McKean Co.: Venereal Clinic, Community Hospital. Free; all venereal diseases.

Kittanning, Armstrong Co.: Kittanning Clinic, Courthouse Annex. Free; all venereal diseases.

Lancaster, Lancaster Co.:

Lancaster General Hospital. Free; all venereal diseases.

St. Joseph's Hospital, 202 College Ave. Free; all venereal diseases.

Latrobe, Westmoreland Co., Latrobe Hospital. Free; syphilis only.

Lebanon, Lebanon Co.: G. U. Clinic, Good Samaritan Hospital. Free; all venereal diseases.

Lewistown, Mifflin Co.: Venereal Disease Clinic, 30 Chestnut St. Free; all venereal diseases.

Lock Haven, Clinton Co.: Venereal Disease Clinic, Lock Haven Hospital, Susquehanna Ave. Free; syphilis only.

McKeesport, Allegheny Co.: McKeesport Hospital, 1501 Fifth Ave. Free and part-pay; all venereal diseases.

McKees Rocks, Allegheny Co.: Ohio Valley Hospital. Free; syphilis only.

Meadville, Crawford Co.: State Clinic, Courthouse. Free; all venereal diseases.

Mifflintown, Juniata Co.: G. U. Clinic. Free; all venereal diseases.

Millersburg, Dauphin Co.: Millersburg Clinic, 403 Union St. Free; syphilis only.

Millvale, Allegheny Co.: Millvale G. U. Clinic, Borough Building. Free; syphilis only.

Monessen, Westmoreland Co.: Monessen Clinic, City Building. Free; all venereal diseases.

Mount Carmel, Northumberland Co.: Mount Carmel Clinic, Victoria Building. Free; syphilis only.

Nanticoke, Luzerne Co.: Nanticoke State Hospital. Part-pay; syphilis only.

New Castle, Lawrence Co.: New Castle Clinic, 11½ East St. Free; all venereal diseases.

New Eagle, Washington Co.: New Eagle Clinic, Memorial Hospital. Free; all venereal diseases.

New Kensington, Westmoreland Co.: New Kensington Clinic, 1156 Fourth Ave. Free; all venereal diseases.

Norristown, Montgomery Co.: State Clinic, Sacred Heart Hospital, Basin and Powell Sts. Free; all venereal diseases.

Oil City, Venango Co.:

Oil City G. U. Clinic, Oil City Hospital. Free; all venereal diseases.

State Clinic, Veach Bldg. Free; syphilis only.

Philadelphia, Philadelphia Co.:

American Oncologic Hospital, 33d St. and Powelton Ave. Free, and pay or part-pay; syphilis only.

Barton Dispensary: 21st St. and North College Ave. Free; syphilis only.

Broad Street Hospital, 739 South Broad St. Free; syphilis only.

Chestnut Hill Hospital, 8835 Germantown Ave. Free, and pay or part-pay; all venereal diseases except gonorrhea in men.

Children's Hospital of Philadelphia, 18th and Bainbridge Sts. Part-pay; all venereal diseases. (Children only.)

Germantown Hospital, Penn and Chew Sts. Part-pay; all venereal diseases.

Frederick Douglas Hospital, 1530 Lombard St. Free; all venereal diseases.

Episcopal Hospital, Front St. and Lehigh Ave. Free and pay; syphilis only.

Genito-urinary Clinic, Frankford Hospital, Frankford Ave. and Wakeling St. Free and part-pay; all venereal diseases.

Syphilis Clinic, Graduate Hospital, 18th and Lombard Sts. Free and part-pay; syphilis only.

Hahnemann Hospital, Broad St. above Race St. Free and part-pay; syphilis only.

Jefferson Hospital, 10th and Sansom Sts. Free and part-pay; syphilis only.

Jewish Hospital, York and Tabor Road St. Part-pay; all venereal diseases.

Kensington Hospital for Women, 136 West Dramond St. (Women only.) Free, and pay or part-pay; syphilis and gonorrhea only.

Lankenau Hospital, Girard and Corinthian Aves. (Children only.) Free, and pay or part-pay; all venereal diseases.

Memorial Hospital, 5800 Ridge Ave. Free, and pay or part-pay; all venereal diseases.

Mercy Hospital, 5000 Woodland Ave. Free; syphilis only.

Methodist Episcopal Hospital, Broad and Wolf Sts. Part-pay; syphilis only.

Mount Sinai Hospital, Fifth and Reed Sts. Free, and pay or part-pay; all venereal diseases.

Northeastern Hospital, Allegheny Ave. and Tulip St. Free, and pay or part-pay; all venereal diseases.

Northern Liberties Hospital, 7th and Brown Sts. Free; all venereal diseases.

Pennsylvania Hospital, 8th and Spruce Sts. Free, and pay or part-pay; syphilis and gonorrhea only.

Philadelphia Italian Hospital, 10th and Carpenter Sts. Free; syphilis only.

St. Agnes Hospital, Broad and Miffin Sts. Part-pay; all venereal diseases.

Philadelphia, Philadelphia Co.—Continued.

St. Christopher's Hospital for Children, Lawrence and Huntingdon Sts. Free, and pay or part-pay; all venereal diseases (children up to 14 years of age only).

St. Joseph's Hospital, 16th St. and Girard Ave. Free; all venereal diseases.

St. Luke's Hospital, 8th and Thompson Sts. Free; all venereal diseases.

St. Mary's Hospital, Frankford Ave. and Palmer St. Free; all venereal diseases.

St. Vincent's Hospital, 70th St. and Woodland Ave. Free; all venereal diseases.

The Skin and Cancer Hospital of Philadelphia, 802–808 Pine St. Free, and pay or part-pay; syphilis only.

State Clinic, 1137 South 20th St. Free; syphilis only.

State Clinic, 1129 Callowhill St. Free; syphilis only.

State Clinic, 3713 Haverford Ave. Free; syphilis only.

State Clinic, 2052 Ridge Ave. Free; syphilis only.

Temple Medical School, Temple University Hospital, Broad and Ontario Sts. Part-pay; syphilis only.

University of Pennsylvania Hospital, 34th and Spruce Sts. Part-pay and pay; all venereal diseases except gonorrhea.

Urological Clinic, Presbyterian Hospital, 39th St. and Powelton Ave. Free, and pay or part-pay; all venereal diseases.

Will's Eye Clinic, 16th and Spring Garden Sts. Free and part-pay; syphilis only.

Women's Homeopathic Hospital, 20th St. and Susquehanna Ave. Part-pay; all venereal diseases.

Woman's Hospital, 4035 Parrish St. (Males accepted only in unusual instances.) Free, and pay or part-pay; syphilis only.

Philipsburg, Centre Co.: Philipsburg State Hospital, 16 South Front St. Free; all venereal diseases.

Phoenixville, Chester Co.: Phoenixville Hospital. Free; all venereal diseases.

Pittsburgh, Allegheny Co.:

Allegheny General Hospital, 320 East North Ave. Free and part-pay; all venereal diseases.

Belvedere Hospital, 801 Paulson Ave. (East Liberty). Free; all venereal diseases.

Center Avenue Health Clinic, 2405 Center Ave. (Children only.) Free; syphilis only.

Children's Hospital, 127 De Soto St. (Children only.) Free and part-pay; syphilis only.

Falk Clinic, 3601 Fifth Ave. (Adults only.) Free and part-pay; all venereal diseases.

Magee Hospital, Forbes and Halket Sts. Free; syphilis only.

Mercy Hospital, Pride and Locust Sts. Free and part-pay; syphilis only.

Montefiore Hospital, 3459 Fifth Ave. Free; all venereal diseases.

Passavant Dispensary, Roberts and Reed Sts. Free and part-pay; syphilis only.

Pittsburgh Hospitals Association, Frankstown Ave. and Washington Blvd. Part-pay; all venereal diseases.

St. Francis Hospital, Forty-fifth St. Free; all venereal diseases.

St. John's General Hospital, 3339 McClure Ave., N. S. Free; syphilis only.

Pittsburgh, Allegheny Co.—Continued.

St. Margaret Memorial Hospital, 46th St. Free; all venereal diseases.

Shadyside Clinic, Center Ave. Free; syphilis only.

Skin and Cancer Foundation, 4518 Winthrop St. Free and part-pay; syphilis only.

South Side Hospital, South 20th St. Free; all venereal diseases.

Western Pennsylvania Hospital, Friendship Ave. Free; all venereal diseases.

Pittston, Luzerne Co.: Pittston Hospital. Free; syphilis only.

Point Marion, Fayette Co.: Point Marion Clinic. Municipal Bldg. Free; all venereal diseases.

Pottstown, Montgomery Co.: Pottstown Hospital. Free; all venereal diseases.

Pottsville, Schuylkill Co.: Pottsville Hospital. Part-pay; all venereal diseases.

Punxsutawney, Jefferson Co.: State Clinic, Farmers & Miners Trust Bldg. (White only.) Free; syphilis only.

Quakertown, Bucks Co.: Community Hospital, 11th St. and Park Ave. Free; syphilis only.

Reading, Berks Co.:

Homeopathic Hospital, 135 North 6th St. Free and part-pay; all venereal diseases.

St. Joseph's Hospital, 12th and Walnut Sts. Part-pay; all venereal diseases.

Renovo, Clinton Co.: Renovo Hospital Annex. Free; all venereal diseases.

Ridley Park, Delaware Co.: Taylor Hospital. Free; syphilis only.

Rochester, Beaver Co.: Rochester General Hospital. Free; all venereal diseases.

Sayre, Bradford Co.: Robert Packer Hospital. Free and part-pay; all venereal diseases.

Scranton, Lackawanna Co.:

The Hahnemann Hospital, Genito-urinary Clinic, 316 Colfax Ave. Free and part-pay; all venereal diseases.

St. Joseph's Children's and Maternity Hospital. Free; all venereal diseases.

State Clinic, 333 Adams Ave. Free; all venereal diseases.

Sewickley, Allegheny Co.: Valley Hospital, Blackburn Road. Free; all venereal diseases.

Shamokin, Northumberland Co.: Pennsylvania State Clinic, 525 North Market St. Free; syphilis only.

Sharon, Mercer Co.: C. H. Buhl Hospital. Free; all venereal diseases.

Shenandoah, Schuylkill Co.: State Clinic, Sweet Building, Main and Lloyd Sts. Free; all venereal diseases.

Somerset, Somerset Co.: Venereal Clinic, Peoples National Bank Building. Free; all venereal diseases.

Spangler, Cambria Co.: Miners' Hospital. (White only.) Free; syphilis only.

Stroudsburg, Monroe Co.: Stroudsburg Clinic, 13 North 6th St. Free; all venereal diseases.

Sunbury, Northumberland Co.: State Clinic, 26 North 4th St. Free; all venereal diseases.

Tyrone, Blair Co.: Tyrone Clinic, Municipal Building, Logan Ave. and 11th St. Free; all venereal diseases.

Uniontown, Fayette Co.: Uniontown Hospital, West Berkeley St. Free; all venereal diseases.

Warren, Warren Co.: G. U. Clinic, 211 Market St. Free; all venereal diseases.

Washington, Washington Co.: Washington Hospital. Free; syphilis and gonorrhea only.

Waynesboro, Franklin Co.: Waynesboro Hospital. Free; all venereal diseases.

Waynesburg, Greene Co.: Venereal Disease Clinic, 25 East High St. Free; all venereal diseases.

Wellsboro, Tioga Co.: Venereal Disease Clinic, Courthouse. Free; all venereal diseases.

West Chester, Chester Co.: Homeopathic Hospital. Free; all venereal diseases.

West Reading, Berks Co.: Reading Clinic. Free and part-pay; syphilis only.

Wilkes-Barre, Luzerne Co.:

General Hospital, North River St. Free, and pay or part-pay; all venereal diseases.

Kirby Health Center, 71 North Franklin St. Free; all venereal diseases.

Mercy Hospital, 196 Hanover St. Free, and pay or part-pay; all venereal diseases.

Wilkinsburg, Allegheny Co.: Columbia Hospital, 312 West St. Free and part-pay; syphilis only.

Williamsport, Lycoming Co.: State Clinic, 625 West Edwin St. Free; all venereal diseases.

Windber, Somerset Co.: Berwind Clinic of the Windber Hospital. Free and pay; all venereal diseases.

York, York Co.: York Hospital. Free; all venereal diseases.

RHODE ISLAND

Bristol, Bristol Co.: Southeast Health Unit, Rockwell House, Hope St. Free; syphilis only.

Newport, Newport Co.: Newport Hospital, Friendship St. Part-pay; all venereal diseases.

Pawtucket, Providence Co.: Memorial Hospital, Prospect St. Free and part-pay; all venereal diseases.

Providence, Providence Co.:

Charles V. Chapin Hospital, 153 Eaton St. Free and part-pay; all venereal diseases.

Rhode Island Hospital, 593 Eddy St. Part-pay; all venereal diseases.

St. Joseph Hospital, Broad and Peace Sts. Free, and pay or part-pay; all venereal diseases.

Wakefield, Washington Co.: South County Hospital. Free; noninfectious syphilis only.

Wickford, Washington Co.: North Kingstown Visiting Nurses headquarters. Free; syphilis only.

Woonsocket, Providence Co.: Woonsocket Hospital, Cass Ave. Free and part-pay; all venereal diseases.

SOUTH CAROLINA

Abbeville, Abbeville Co.: Abbeville Co. Health Department, Courthouse. Free and part-pay; all venereal diseases.

Adams Run, Charleston Co.: Charleston Co. Mobile Unit, Legare (Harmon Clinic). Free; syphilis only.

Aiken, Aiken Co.: Aiken Co. Health Department. Free; all venereal diseases.

Allendale, Allendale Co.: Allendale Co. Health Department. Free; syphilis only.

Alms House, Richland Co.: Richland Co. Mobile Unit, Dentsville. Free and part-pay; syphilis only.

Anderson, Anderson Co.: Anderson Co. Health Department, Courthouse. Free and part-pay; all venereal diseases.

Andrews, Georgetown Co.: Georgetown Co. Masonic Bldg. Free and part-pay; all venereal diseases.

Andrews Yard, Richland Co.:

Richland Co. Mobile Unit, Celcure Company. Free and part-pay; syphilis only.

Richland Co. Mobile Unit, Truesdale Stock Yard. Free and part-pay; syphilis only.

Awendaw, Charleston Co.:

Charleston Co. Mobile Unit, Thomas' Store (12 Mile). Free; syphilis only.

Charleston Co. Mobile Unit, Freeman's Store (15 mile). Free; syphilis only.

Charleston Co. Mobile Unit, Thames' Store (24 Mile). Free; syphilis only.

Ballentine, Richland Co.: Richland Co. Mobile Unit, Chain Gang Camp No. 3. Free and part-pay; syphilis only.

Bamberg, Bamberg Co.: Bamberg Co. Health Department. Free and part-pay; all venereal diseases.

Barnwell, Barnwell Co.: Barnwell Co. Health Department. Free and part-pay; all venereal diseases.

Beaufort, Beaufort Co.: Beaufort Co. Health Department. Free; all venereal diseases.

Bellinger Hill, Beaufort Co.: Beaufort Co. Mobile Unit, Baptist Church. Free; syphilis only.

Bennettsville, Marlboro Co.: Marlboro Co. Health Department. Free; all venereal diseases.

Bethune, Kershaw Co.: Kershaw Co. Health Department, High School Bldg. Free; all venereal diseases.

Big State, Beaufort Co.: Beaufort Co. Mobile Unit, Clinic Bldg. Free; syphilis only.

Bishopville, Lee Co.: Lee Co. Health Department, Courthouse. Free and part-pay; syphilis only.

Blaney, Kershaw Co.: Kershaw Co. Health Department, High School Bldg. Free; all venereal diseases.

Bluffton, Beaufort Co.: Beaufort Co. Health Department, Health Center. Free; all venereal diseases.

Blythewood, Richland Co.:

Richland Co. Mobile Unit, Mr. Wilson's Farm. Free and part-pay; syphilis only.

Richland Co. Mobile Unit, Health Center. Free and part-pay; syphilis only.

Bookman, Richland Co.: Richland Co. Mobile Unit, Mr. Hinnant's Farm. Free and part-pay; syphilis only.

Camden, Kershaw Co.: Kershaw Co. Health Department, Agricultural Bldg. Free; all venereal diseases.

Carlisle, Union Co.: Union Co. Health Department, Colored School. Free and part-pay; all venereal diseases.

Chapin, Lexington Co.: Lexington Co. Health Department, Fulmer's Store. Free and part-pay; syphilis only.

Charleston, Charleston Co.:

Health Department, Health Center Clinic. Free; all venereal diseases.

Negro Hospital and Training School, 135 Cannon St. Free; syphilis only.

Shirra's Dispensary, Roper Hospital, Lucas and Calhoun Sts. Free; all venereal diseases.

Cheraw, Chesterfield Co.: Chesterfield Co. Health Center. Free; all venereal diseases.

Chester, Chester Co.: Chester Co. Health Department, Courthouse. Free and part-pay; syphilis only.

Chesterfield, Chesterfield Co.: Chesterfield Co. Health Department, Courthouse. Free; all venereal diseases.

Clemson, Pickens Co.: Clemson-Calhoun Health Center. Pay; syphilis only.

Clinton, Laurens Co.: Laurens Co. Health Department, City Hall. Free and part-pay; all venereal diseases.

Clio, Marlboro Co.: Marlboro Co. Health Office. Free: all venereal diseases.

Columbia, Richland Co.:

Richland Co. Mobile Unit, Arthurtown, Columbia Dairies. Free and part-pay; syphilis only.

Richland Co. Mobile Unit, Colonial Heights, Swindler's Dairy. Free and part-pay; syphilis only.

Richland Co. Cola-Richland Co. Venereal Clinic. 1209½ Lady St. Free and part-pay; all venereal diseases.

Congaree, Richland Co.: Richland Co. Mobile Unit, R. R. Depot. Free and part-pay; syphilis only.

Congaree Acres, Richland Co.: Richland Co. Mobile Unit, Dr. Weston's Farm. Free and part-pay; syphilis only.

Conway, Horry Co.: Horry Co. Health Department, Community Center. Part-pay; syphilis only.

Cross, Berkeley Co.: Berkeley Co. Health Department, Jehovah Church. Free; all venereal diseases.

Dale, Beaufort Co.: Beaufort Co. Health Department, Health Center. Free; all venereal diseases.

Daufuskie Island, Beaufort Co.: Beaufort Co. Mobile Unit, Merry Field School. Free; syphilis only.

Darlington, Darlington Co.: Darlington Co. Health Department, Courthouse. Free and part-pay; all venereal diseases.

Dillion, Dillon Co.: Dillon Co. Health Department, Courthouse. Free and part-pay; syphilis only.

Eastover, Richland Co.:

Richland Co. Mobile Unit, Chain Gang Camp No. 1. Free and part-pay; syphilis only.

Richland Co. Mobile Unit, Medical Center. Free and part-pay; syphilis only.

Edgefield, Edgefield Co.: Edgefield Co. Health Department, Court house. Free and part-pay; all venereal diseases.

Edisto Island, Charleston Co.: Charleston Co. Mobile Unit, Posner's Store. Free; syphilis only.

Enoree, Spartanburg Co.: Enoree Mill Clinic. Free and part-pay; syphilis only.

Estill, Hampton Co.: Hampton Co. Health Department, Town Hall. Free; all venereal diseases.

Fairwold, Richland Co.:

Richland Co. Mobile Unit, Conder's Barn. Free and part-pay; syphilis only.

Richland Co. Mobile Unit, Fairwold Dairy Farm. Free and part-pay; syphilis only.

Florence, Florence Co.: Florence Clinic, Courthouse. Part-pay; syphilis only.

Fort Mill, York Co.: York Co. Health Department, Branch Health Office, Main St. Free; syphilis only.

Fort Motte, Calhoun Co.: Calhoun Co. Health Department, Weeks' Bldg. Free and part-pay; all venereal diseases.

Fountain Inn, Greenville Co.: Greenville Co. Health Department, Main St. Drugstore Bldg. Free and part-pay; all venereal diseases.

Fregmore, Beaufort Co.: Beaufort Co. Health Department, St. Helena's Island, Dr. Bailey's Office. Part-pay; syphilis only.

Gadsden, Richland Co.: Richland Co. Mobile Unit, Scott's General Store. Free and part-pay; syphilis only.

Gaffney, Cherokee Co.: Cherokee Co. Health Department, Courthouse. Free; all venereal diseases.

Georgetown, Georgetown Co.: Georgetown Co. Health Department, City Hall. Free and part-pay; all venereal diseases.

Green Pond, Colleton Co.: Colleton Co. Mobile Unit, Clinic Bldg. Free; syphilis only.

Greenville, Greenville Co.:

Greenville City Clinic, City Hall Bldg., Main St. Part-pay; all venereal diseases.

Greenville Co. Venereal Clinic, 13 West Court St. Free and part-pay; all venereal diseases.

Greenwood, Greenwood Co.: Greenwood Co. Health Department, 515 Main St. Free; all venereal diseases.

Hardeeville, Jasper Co.: Jasper Co. Clinic, City Hall. Free; syphilis only.

Hartsville, Darlington Co.: Darlington Co. Clinic, Community Bldg. Free and part-pay; all venereal diseases.

Hilton Head Island, Beaufort Co.: Beaufort Co. Mobile Unit, Chaplin School Bldg. Free; syphilis only.

Hopkins, Richland Co.: Richland Co. Mobile Unit, Gorman's Store. Free and part-pay; syphilis only.

Jacksonboro, Colleton Co.: Colleton Co. Clinic, Colored Church. Free; all venereal diseases.

James Island, Charleston Co.: Charleston Co. Mobile Unit, Coker's Store. Free; syphilis only.

John's Island, Charleston Co.:

Charleston Co. Mobile Unit, Howell's Store. Free; syphilis only.

Charleston Co. Mobile Unit, Hebron Church. Free; syphilis only.

Charleston Co. Mobile Unit, Limehouse Store. Free; syphilis only.

Charleston Co. Mobile Unit, Mr. Smith's Store, (Red Top). Free; syphilis only.

Charleston Co. Mobile Unit, Tucker's Store, (on Rockville Road). Free; syphilis only.

Johnston, Edgefield Co.: Edgefield Co. Health Department, Johnston Colored School House. Free and part-pay; all venereal diseases.

Kingville, Richland Co.: Richland Co. Mobile Unit, Holly Hill Lumber Co. Free; syphilis only.

Kingstree, Williamsburg Co.: Williamsburg Co. Health Department. Free and part-pay; all venereal diseases.

Lake View, Dillon Co.: Dillon Co. Health Department, Lake View Pharmacy. Free and part-pay; syphilis only.

Lamar, Darlington Co.: Darlington Co. Health Department, Lamar Clinic. Free and part-pay; all venereal diseases.

Lancaster, Lancaster Co.: Lancaster Co. Health Department, County Office Bldg. Free and part-pay; all venereal diseases.

Latta, Dillon Co.: Dillon Co. Clinic, Blum Bldg. Free and part-pay; syphilis only.

Laurens, Laurens Co.: Laurens Co. Health Department. Free and part-pay; all venereal diseases.

Leesville, Lexington Co.: Lexington Co. Health Department, Leesville Clinic, Town Hall. Free and part-pay; syphilis only.

Levy, Beaufort Co.: Beaufort Co. Mobile Unit, Zion Society Hall. Free; syphilis only.

Lexington, Lexington Co.: Lexington Co. Health Department, Agricultural Bldg. Free and part-pay; syphilis only.

Liberty Hill, Charleston Co.: Charleston Co. Mobile Unit, Colored School. Free; syphilis only.

Lone Star, Calhoun Co.: Calhoun Co. Health Department, Over Murray's Store. Free and part-pay; all venereal diseases.

Loris, Horry Co.: Horry Co. Health Department, Gateway Drug Company. Part-pay; syphilis only.

Lykesland, Richland Co.:

Richland Co. Mobile Unit, Mr. Burnside's Farm. Free and part-pay; syphilis only.

Richland Co. Mobile Unit, Consolidated High School. Free and part-pay; syphilis only.

Richland Co. Mobile Unit, Medical Center. Free and part-pay; syphilis only.

Lynchburg, Lee Co.: Lee Co. Health Department, Lynchburg Clinic, Bank Bldg. Free and part-pay; syphilis only.

Manning, Clarendon Co.: Clarendon Co. Health Department, Courthouse. Free and part-pay; all venereal diseases.

Marion, Marion Co.: Marion Co. Health Department. Free and part-pay; all venereal diseases.

McClellanville, Charleston Co.: Charleston Co. Mobile Unit, Mr. Beckman's Office. Free; syphilis only.

McColl, Marlboro Co.: Marlboro Co. Health Department, Health Office. Free; all venereal diseases.

McCormick, McCormick Co.: McCormick Co. Health Department, Courthouse. Free; syphilis only.

Meeting Street Road, Charleston Co.: Charleston Co. Mobile Unit, Hackermann's Store. Free; syphilis only.

Meggetts, Charleston Co.: Charleston Co. Mobile Unit, Anivester Church. Free; syphilis only.

Midland Park, Charleston Co.: Charleston Co. Mobile Unit, Stall's Store. Free; syphilis only.

Moncks Corner, Berkeley Co.: Berkeley Co. Health Department. Free; all venereal diseases.

Mullins, Marion Co.: Marion Co. Health Department, Over Martin's Drugstore. Free and part-pay; all venereal diseases.

Mt. Pleasant, Charleston Co.: Charleston Co. Mobile Unit, 4 Mile Church. Free; syphilis only.

Myrtle Beach, Horry Co.: Horry Co. Health Department, White High School Bldg. Part-pay; syphilis only.

Newberry, Newberry Co.: Newberry Co. Health Department, Exchange Bank Bldg. Free; syphilis only.

Old Winnsboro Road, Richland Co.: Richland Co. Mobile Unit, Chain Gang Camp No. 4. Free and part-pay; syphilis only.

Orangeburg, Orangeburg Co.: Orangeburg Co. Health Department, County Office Bldg. Free; all venereal diseases.

Parker's Ferry, Charleston Co.: Charleston Co. Mobile Unit, Cross Roads. Free; syphilis only.

Parris Island, Beaufort Co.: Beaufort Co. Health Department, Station Hospital. Free; all venereal diseases.

Pawley's Island, Georgetown Co.: Georgetown Co. Health Department, Health Station. Free and part-pay; all venereal diseases.

Piney Grove, Richland Co.: Richland Co. Mobile Unit, School House. Free and part-pay; syphilis only.

Pineville, Berkeley Co.: Berkeley Co. Health Department, Redeemer Church. Free; all venereal diseases.

Pontiac, Richland Co.: Richland Co. Mobile Unit, Sand Hill Experimental Station. Free and part-pay; syphilis only.

Prosperity, Newberry Co.: Newberry Co. Health Department, Masonic Bldg. Free; syphilis only.

Rantowles, Charleston Co.: Charleston Co. Mobile Unit, Pratt's Esso Station. Free; syphilis only.

Ravenel, Charleston Co.: Charleston Co. Mobile Unit, Post Office. Free; syphilis only.

Richburg, Chester Co.: Chester Co. Health Department, Negro Lodge. Free; syphilis only.

Richtex, Richland Co.: Richland Co. Mobile Unit, Richtex Shale Co. Free and part-pay; syphilis only.

Ridgeland, Jasper Co.: Jasper Co. Health Department, Agricultural Bldg. Free; all venereal diseases.

Ridge Spring, Saluda Co.: Saluda Co. Health Department, Colored School House. Free and part-pay; all venereal diseases.

Ridgewood, Richland Co.: Richland Co. Venereal Clinic, Bus Terminal. Free and part-pay syphilis only.

Ruffin, Colleton Co.: Colleton Co. Health Department, Colored Church. Free; all venereal diseases.

Saluda, Saluda Co.: Saluda Co. Health Department, Courthouse. Free and part-pay; all venereal diseases.

Santee, Charleston Co.: Charleston Co. Mobile Unit, Solomon's Store. Free; syphilis only.

Seneca, Oconee Co.: Oconee Co. Health Department, Seneca Clinic, City Hall. Free; syphilis only.

Sheldon, Beaufort Co.: Beaufort Co. Mobile Unit, Colored School Bldg. Free; syphilis only.

Spartanburg, Spartanburg Co.:

Spartanburg City Health Department, City Hall. Free; syphilis only.

Spartanburg Co. Health Department. Free; syphilis only.

Spartanburg General Hospital, 891 North Church St. Free; syphilis only.

St. George, Dorchester Co.: Dorchester Co. Health Department. Free; all venereal diseases.

St. Matthews, Calhoun Co.: Calhoun Co. Health Department, Agricultural Bldg. Free and part-pay; all venereal diseases.

State Park, Richland Co.: Richland Co. Mobile Unit, Dr. Cooper's Store. Free and part-pay; syphilis only.

Summerville, Dorchester Co.: Dorchester Co. Health Department, City Bldg. Free; all venereal diseases.

Sumter, Sumter Co.:
Sumter City Health Department, 8 Caldwell St. Free and part-pay; all venereal diseases.
Sumter Co. Health Department, Courthouse. Free and part-pay; all venereal diseases.

Taylors, Richland Co.: Richland Co. Mobile Unit, Swifts Oil Mill. Free and part-pay; syphilis only.

Tillman, Jasper Co.: Jasper Co. Health Department, Ritter Lumber Co. Office. Free; all venereal diseases.

Trenton, Edgefield Co.: Edgefield Co. Health Department, Colored School Bldg. Free and part-pay; all venereal diseases.

Twin Lakes, Richland Co.: Richland Co. Mobile Unit, Chain Gang Camp No. 2. Free and part-pay; syphilis only.

Union, Union Co.:
Union Co. Chain Gang Camp. Free; all venereal diseases.
Union Co. Health Department, Kirby Bldg. Free and part-pay; all venereal diseases.

Van Wyck, Lancaster Co.: Lancaster Co. Health Department, Brick Yard Office. Part-pay; all venereal diseases.

Varnville, Hampton Co.: Hampton Co. Health Department, Health Center. Free; all venereal diseases.

Wadmalaw Island, Charleston Co.: Charleston Co. Mobile Unit, Bethlehem Baptist Church. Free; syphilis only.

Wagener, Aiken Co.: Aiken Co. Health Department, Health Center. Free; all venereal diseases.

Walhalla, Oconee Co.: Oconee Co. Health Department. Free; syphilis only.

Walterboro, Colleton Co.: Colleton Co. Health Department. Free; all venereal diseases.

Wando, Berkeley Co.: Berkeley Co. Health Department, St. Stephen's Church. Free; all venereal diseases.

West Columbia, Lexington Co.: Lexington Co. Health Department, Town Hall. Free and part-pay; syphilis only.

Westminster, Oconee Co.: Oconee Co. Health Department, City Hall. Free; syphilis only.

Winnsboro, Fairfield Co.: Fairfield Co. Health Department, Courthouse. Free and part-pay; all venereal diseases.

Yemassee, Hampton Co.: Hampton Co. Mobile Unit, Colored School Bldg. Free; syphilis only.

SOUTH DAKOTA

Sioux Falls, Minnehaha Co.: City Health Department. Free; syphilis only.

NOTE.—The venereal disease control program of South Dakota is based on a plan of payments made to private physicians for the treatment of venereal diseases in indigent patients. While only one clinic is functioning, the addresses of physicians giving treatment for venereal diseases under the State plan may be obtained from State, county, and municipal health officers.

TENNESSEE

Alamo, Crockett Co.: Alamo Clinic. Free; all venereal diseases.

Arlington, Shelby Co.:
Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Arlington Depot. (White only.) Free; all venereal diseases.

Arlington, Shelby Co.—Continued.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, S. Y. Wilson's Store. (Negro only.) Free; all venereal diseases.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Porter's Store. (Negro only.) Free; all venereal diseases.

Athens, McMinn Co.: McMinn Co. Health Unit. Free; all venereal diseases.

Barretville, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit. Barret's Store. Free; all venereal diseases.

Bartlett, Shelby Co.:

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Breathett Undertaker's Parlor. (Negro only.) Free; all venereal diseases.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Schwam's Store. (White only.) Free; all venereal diseases.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Oakgrove Colored School. (Negro only.) Free; all venereal diseases.

Bells, Crockett Co.: Bells Clinic. Free; all venereal diseases.

Bickford Station, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Benjestown Colored School. (Negro only.) Free; all venereal diseases.

Berclair, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Berclair Community Center. Free; all venereal diseases.

Birchwood, Hamilton Co.: Birchwood Health Center. Free; all venereal diseases.

Blountville, Sullivan Co.: Blountville Clinic. Free; syphilis only.

Bolivar, Hardeman Co.: Venereal Disease Clinic. Free; all venereal diseases.

Bolton, Shelby Co.:

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Pearlie's Store. Free; all venereal diseases.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Smith and Osborne's Store. Free; all venereal diseases.

Bradford, Gibson Co.: Gibson Co. Health Department. Free; all venereal diseases.

Bristol, Sullivan Co.: Bristol Clinic. Free; syphilis only.

Brunswick, Shelby Co.:

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Brunswick Colored School. (Negro only.) Free; all venereal diseases.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Shelton's Store. (White only.) Free; all venereal diseases.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Sanderlin's Store. (Negro only.) Free; all venereal diseases.

Byrdstown, Pickett Co.: Pickett Co. Health Department. Free; all venereal diseases.

Capleville, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Capleville Colored School. (Negro only.) Free; all venereal diseases.

Celina, Clay Co.: Celina Clinic. Free; all venereal diseases.

Centerville, Hickman Co.: Hickman Co. Clinic. Free; all venereal diseases.

Chattanooga, Hamilton Co.:

Venereal Disease Clinic, Erlanger Hospital. (Adults only.) Free; all venereal diseases.

Tennessee Valley Authority Clinic, 101 Pound Bldg. (Adults only.) Free; syphilis only.

Tennessee Valley Authority, Chickamauga Dam. (Adults only.) Free; syphilis only.

Clarksville, Montgomery Co.: Montgomery Co. Health Department, Venereal Disease Clinic. Free; all venereal diseases.

Cleveland, Bradley Co.: Bradley Co. Clinic. Free; all venereal diseases.

Clinton, Anderson Co.: Venereal Clinic, Broad St. Free; all venereal diseases.

College Grove, Williamson Co.: Williamson Co. Health Department. Free; all venereal diseases.

Collierville, Shelby Co.: Collierville Clinic. Free; all venereal diseases.

Columbia, Maury Co.: Maury Co. Health Department, Courthouse. Free; all venereal diseases.

Cordova, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Cordova Depot. Free; all venereal diseases.

Covington, Tipton Co.: Tipton Co. Health Department, Venereal Clinic. Free; all venereal diseases.

Crossville, Cumberland Co.: Cumberland Co. Venereal Disease Clinic. Free; all venereal diseases.

Cuba, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Sigler's Store. Free; all venereal diseases.

Dayton, Rhea Co.: Dayton Clinic. Free; all venereal diseases.

Decatur, Meigs Co.: Rhea-Meigs Clinic. Free; all venereal diseases.

Decaturville, Decatur Co.: Decatur Co. Health Department. Free; all venereal diseases.

Dellrose, Lincoln Co.: Lincoln Co. Health Department. Free; all venereal diseases.

Douglas, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Douglas Colored School. (Negro only.) Free; all venereal diseases.

Dresden, Weakley Co.: Dresden Clinic. Free; all venereal diseases.

Dunlap, Sequatchie Co.: Dunlap Clinic. Free; all venereal diseases.

Dyersburg, Dyer Co.: Dyersburg Clinic, Cedar St. Free; all venereal diseases.

Eads, Shelby Co.:

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Richmond's Store. Free; all venereal diseases.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Riggin's Store. (Negro only.) Free; all venereal diseases.

Elizabethton, Carter Co.: Carter Co. Health Department. Free; all venereal diseases.

Ellendale, Shelby Co.:

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Fullview Church. (Negro only.) Free; all venereal diseases.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Herring's Store. (White only.) Free; all venereal diseases.

Erin, Houston Co.: Venereal Disease Clinic. Free; all venereal diseases.

Erwin, Unicoi Co.: Unicoi Co. Clinic, 102 Tucker St. Free; all venereal diseases.

Etowah, McMinn Co.: McMinn Co. Health Department. Free; all venereal diseases.

Fayetteville, Lincoln Co.: Lincoln Co. Health Department. Free; all venereal diseases.

Felt's Station, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Oberle's Store. (Negro only.) Free; all venereal diseases.

Fisherville, Shelby Co.:

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Brigg's Store. Free; all venereal diseases.

Fisherville, Shelby Co.—Continued.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Hamner's Store. Free; all venereal diseases.

Forest Hill, Shelby Co.:

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Forest Hill Colored School. (Negro only.) Free; all venereal diseases.

Memphis- Shelby Co. V. D. Control Project, Mobile Unit, King's Store. (White only.) Free; all venereal diseases.

Franklin, Williamson Co.: Williamson Co. Health Department. Free; all venereal diseases.

Frayser, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Pesthouse. Free; all venereal diseases.

Friendship, Crockett Co.: Friendship Clinic. Free; all venereal diseases.

Gainesboro, Jackson Co.: Gainesboro Clinic. Free; all venereal diseases.

Gallatin, Sumner Co.: Sumner Co. Health Department, 107 Franklin St. Free; all venereal diseases.

Germantown, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Germantown Depot. Free; all venereal diseases.

Gragg, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Eastland Presbyterian Church. (White only.) Free; all venereal diseases.

Greeneville, Greene Co.: Greene Co. (Venereal Disease) Health Department. Free; all venereal diseases.

Greenfield, Weakley Co.: Greenfield Clinic. Free; all venereal diseases.

Halls, Lauderdale Co.: Lauderdale Co. Health Department. Free; all venereal diseases.

Hartsville, Trousdale Co.: Trousdale Co. Clinic. Free; all venereal diseases.

Hixson, Hamilton Co.: Hixson Health Center. Free; all venereal diseases.

Humboldt, Gibson Co.: Gibson Co. Health Department. Free; all venereal diseases.

Irine, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Hack's Cross Road and Shelby Drive. Free; all venereal diseases.

Jamestown, Fentress Co.: Fentress Co. Venereal Disease Clinic. Free; all venereal diseases.

Jellico, Campbell Co.: Jellico V. D. Clinic, City Hall. Free; all venereal diseases.

Johnson City, Washington Co.: Johnson City Clinic, Municipal Bldg. Free; all venereal diseases.

Jonesboro, Washington Co.: Jonesboro Clinic. Free; all venereal diseases.

Kenton, Gibson Co.: Gibson Co. Health Department. Free; all venereal diseases.

Kerrville, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Bethlehem Colored School. (Negro only.) Free; all venereal diseases.

Kingsport, Sullivan Co.: Kingsport Clinic. Free; syphilis only.

Kingston, Roane Co.: Roane Co. Health Department. Free; syphilis only.

Knoxville, Knox Co.:

Venereal Disease Clinic, 619 West Clinch St. (White only.) Free; all venereal diseases.

Venereal Disease Clinic, 211 State St. (Negro only.) Free; all venereal diseases.

Knox Co. Clinic, Courthouse. Free; all venereal diseases.

Knoxville Medical Unit, Health Safety Department, Tennessee Valley Authority, 101 New Sprankle Bldg. (Adults only.) Free; syphilis only.

LaFollette, Campbell Co.: LaFollette Clinic, Tennessee Ave. Free; all venereal diseases.

Lebanon, Wilson Co.: Wilson Co. Health Department. Free; all venereal diseases.
Lenow, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Mount Pisgah Colored School. (Negro only.) Free; all venereal diseases.
Lewisburg, Marshall Co.: Marshall Co. Health Department. Free; all venereal diseases.
Lexington, Henderson Co.: Henderson Co. Health Department. Free; all venereal diseases.
Livingston, Overton Co.: Overton Co. Health Department. Free; all venereal diseases.
Locke, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Gayden's Store. Free; all venereal diseases.
Lucy, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Syke's Store. Free; all venereal diseases.
Lynnville, Giles Co.: Venereal Disease Clinic. Free; all venereal diseases.
Madisonville, Monroe Co.: Madisonville Clinic, County Health Department. Free; syphilis only.
Martin, Weakley Co.: Martin Clinic. Free; all venereal diseases.
Maryville, Blount Co.: Blount Co. Health Department, Gamble Bldg. Free; syphilis only.
Mason, Tipton Co.: Tipton Co. Health Department, Venereal Disease Clinic. Free; all venereal diseases.
Memphis, Shelby Co.:
Shelby Co. Penal Farm Clinic. (Adults only.) Free; all venereal diseases.
Shelby Co. Hospital. (Adults only.) Free; all venereal diseases.
John Gaston Hospital. Free; all venereal diseases.
North Memphis Clinic. (Negro only.) Free; all venereal diseases.
South Memphis Health Center. Free; all venereal diseases.
Court Clinic, 103 B Courthouse. (Adults only.) Free; all venereal diseases.
Beale St. Clinic. (Negro only.) Free; all venereal diseases.
Milan, Gibson Co.: Gibson Co. Health Department. Free; all venereal diseases.
Millington, Shelby Co.:
Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Millington Colored School. (Negro only.) Free; all venereal diseases.
Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Harrell's Store. (White only.) Free; all venereal diseases.
Morris Chapel, Hardin Co.: Hookers Bend Clinic. Free; all venereal diseases.
Morristown, Hamblen Co.: Hamblen Co. Health Department. Free; all venereal diseases.
Moscow, Fayette Co.: Moscow Clinic. Free; all venereal diseases.
Mountain City, Johnson Co.: Johnson Co. Clinic. Free; all venereal diseases.
Mullins Station, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Bridgewater Colored School. (Negro only.) Free; all venercal diseases.
Murfreesboro, Rutherford Co.: Rutherford Hospital. Free; syphilis only.
Nance Bend, Hardin Co.: Nance Bend Clinic. Free; all venereal diseases.
Nashville, Davidson Co.:
City Health Department V. D. Clinic, 801 Demonbreum St. Free; all venereal diseases.
County Health Department, Courthouse. Free; all venereal diseases.
Hubbard Hospital, 18th Ave. North. (Negro adults only.) Part-pay; syphilis only.
State Training School Venereal Disease Clinic. Free; all venereal diseases.

Nashville, Davidson Co.—Continued.

Vanderbilt University Hospital, 21st Ave. South. (Adults only.) Free and pay or part-pay; syphilis only.

Newbern, Dyer Co.: Newbern Clinic. Free; all venereal diseases.

Newport, Cooke Co.: Cooke Co. Clinic. Free; all venereal diseases.

Nolensville, Williamson Co.: Williamson Co. Health Department. Free; all venereal diseases.

Oakville, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Oakville Colored School. (Negro only.) Free; all venereal diseases.

Obion, Obion Co.: Obion Co. Health Department. Free; all venereal diseases.

Ooltewah, Hamilton Co.: Ooltewah Health Center. Free; all venereal diseases.

Parsons, Decatur Co.: Decatur Co. Health Department. Free; all venereal diseases.

Petersburg, Lincoln Co.: Lincoln Co. Health Department. Free; all venereal diseases.

Pikesville, Bledsoe Co.: Pikeville Clinic. Free; all venereal diseases.

Portland, Sumner Co.: Sumner Co. Health Department. Free; all venereal diseases.

Pulaski, Giles Co.: Venereal Disease Clinic, East Madison St. Free; all venereal diseases.

Raleigh, Shelby Co.:

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Gordon's Store. Free; all venereal diseases.

Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Spring Hill Church. (Negro only.) Free; all venereal diseases.

Ridgely, Lake Co.: Ridgely V. D. Clinic. Free; all venereal diseases.

Ripley, Lauderdale Co.: Lauderdale Co. Health Department. Free; all venereal diseases.

Rockwood, Roane Co.: Roane Co. Health Department. Free; syphilis only.

Rogersville, Hawkins Co.: Rogersville Clinic. Free; all venereal diseases.

Rosemark, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Rosemark White School. (White only.) Free; all venereal diseases.

Rossville, Fayette Co.: Johnson Store Clinic, Route 1. Free; all venereal diseases.

Rutherford, Gibson Co.: Gibson Co. Health Department. Free; all venereal diseases.

Rutledge, Grainger Co.: Grainger Co. Venereal Disease Clinic. Free; all venereal diseases.

Saltillo, Hardin Co.: Saltillo Clinic. Free; all venereal diseases.

Savannah, Hardin Co.: Savannah Clinic. Free; all venereal diseases.

Sevierville, Sevier Co.: Sevier Co. Health Department. Free; all venereal diseases.

Sharon, Weakley Co.: Sharon Clinic. Free; all venereal diseases.

Smyrna, Rutherford Co.: Rutherford Co. Venereal Disease Clinic. Free; syphilis only.

Soddy, Hamilton Co.: Soddy Health Center. Free; all venereal diseases.

Somerville, Fayette Co.: Somerville V. D. Clinic. Free; all venereal diseases.

Summit, Hamilton Co.: Summit Health Center. Free; all venereal diseases.

Sweetwater, Monroe Co.: Monroe Co. Health Department, Sweetwater Clinic. Free; syphilis only.

Tazewell, Claiborne Co.: Tazewell Clinic. Free; all venereal diseases.

Tiptonville, Lake Co.: Tiptonville V. D. Clinic. Free; all venereal diseases.

Tracy City, Grundy Co.: Venereal Disease Clinic. Free; all venereal diseases.
Trenton, Gibson Co.: Gibson Co. Health Department. Free; all venereal diseases.
Trimble, Dyer Co.: Trimble Clinic. Free; all venereal diseases.
Tullahoma, Coffee Co.: Coffee Co. Clinic, Vocational School for Girls. (White only; children only.) Free; all venereal diseases.
Tully Station, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Tully's Store. (Negro only.) Free; all venereal diseases.
Union City, Obion Co.: Obion Co. Health Department, Third St. Free; all venereal diseases.
Union Valley, Williamson Co.: Williamson Co. Health Department. Free; all venereal diseases.
Wartburg, Morgan Co.: Morgan Co. Venereal Disease Clinic. Free; all venereal diseases.
Watts Bar Dam, Rhea Co.: Venereal Disease Clinic. Free; all venereal diseases.
Waverly, Humphreys Co.: Venereal Disease Clinic. Free; all venereal diseases.
Weaver, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Weaver School. (Negro only.) Free; all venereal diseases.
West Junction, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Martin's Store. Free; all venereal diseases.
Westmoreland, Sumner Co.: Sumner Co. Health Department. Free; all venereal diseases.
Whitehaven, Shelby Co.:
Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Hilderbrand's Store. Free; all venereal diseases.
Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Geeter Colored School. (Negro only.) Free; all venereal diseases.
White Station, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Scott's Grocery. (Negro only.) Free; all venereal diseases.
Winchester, Franklin Co.: Franklin Co. Health Department. Free; all venereal diseases.
Woodstock, Shelby Co.: Memphis-Shelby Co. V. D. Control Project, Mobile Unit, Woodstock Colored School. (Negro only.) Free; all venereal diseases.

TEXAS

Abilene, Taylor Co.: Abilene-Taylor Clinic, Courthouse. Free; all venereal diseases.
Atlanta, Cass Co.: Cass Co. Clinic. Free; all venereal diseases.
Austin, Travis Co.: Austin-Travis Clinic, Breckenridge Hospital. Free; all venereal diseases.
Beaumont, Jefferson Co.: Beaumont V. D. Clinic, 855 Trinity St. Free; all venereal diseases.
Beeville, Bee Co.: Bee Co. Clinic. Free; all venereal diseases.
Big Spring, Howard Co.: Big Spring Clinic, V. D. Clinic Bldg. Free; all venereal diseases.
Brownsville, Cameron Co.: Cameron Co. Clinic, City Hall. Free; all venereal diseases.
Bryan, Brazos Co.: Brazos-Bryan Clinic, City Hall. Free; all venereal diseases.
Canutillo; El Paso Co.: Canutillo Clinic, Health Department Bldg. Free; all venereal diseases.
Clint, El Paso Co.: Clint Clinic, Health Department Bldg. Free; all venereal diseases.

Coleman, Coleman Co.: Coleman Co. Clinic, Overall Hospital. Free; all venereal diseases.

Cooper, Delta Co.: Delta Co. Clinic, James Hospital. Free; all venereal diseases.

Corpus Christi, Nueces Co.: Corpus Christi Clinic, Clinic Building. Free; all venereal diseases.

Dallas, Dallas Co.: Dallas Co. Clinic, Parkland Hospital. Free; all venereal diseases.

De Kalb, Bowie Co.: De Kalb Clinic, Old Federal Bldg. Free; all venereal diseases.

Del Rio, Val Verde Co.: Del Rio Clinic, Main St. Free; all venereal diseases.

Edinburg, Hidalgo Co.: Hidalgo Co. Clinic. Free; all venereal diseases.

El Paso, El Paso Co.: El Paso Co. Clinic, Health Center No. 1, % Health Unit. Free; all venereal diseases.

Fabens, El Paso Co.: Fabens Clinic. Free; all venereal diseases.

Fort Worth, Tarrant Co.: Fort Worth Clinic, 315 East 5th St. Free; all venereal diseases.

Gainesville, Cooke Co.: Gainesville Clinic, Courthouse. Free; all venereal diseases.

Galveston, Galveston Co.: University of Texas, John Sealy Hospital. Free; all venereal diseases.

Goose Creek, Harris Co.: Tri-Cities Welfare League, Lillie-Duke Hospital. Free; all venereal diseases.

Greenville, Hunt Co.: Greenville Clinic, Courthouse. Free; all venereal diseases.

Harlingen, Cameron Co.: Harlingen Clinic, City Hall. Free; all venereal diseases.

Hemphill, Sabine Co.: Hemphill Clinic, County Nurse's Office. Free; all venereal diseases.

Hillsboro, Hill Co.: Clinic, Courthouse. Free; all venereal diseases.

Houston, Harris Co.:

Health Center No. I, % City Health Department. Free; all venereal diseases.
Health Center No. II, % City Health Department. Free; all venereal diseases.
Houston Clinic, Old Jeff Davis Hospital. Free; all venereal diseases.

Jasper, Jasper Co.: Jasper-Newton Co. Clinic, Health Unit Bldg. Free; all venereal diseases.

Kountz, Hardin Co.: Kountz Clinic, County Nurse's Office. Free; all venereal diseases.

Laredo, Webb Co.: Laredo Clinic, City Hall Annex. Free; all venereal diseases.

Linden, Case Co.: Linden Co. Venereal Disease Clinic, City Hall Annex. Free; all venereal diseases.

Longview, Gregg Co.: Longview Clinic, Health Department Bldg. Free; all venereal diseases.

Lufkin, Angelina Co.: Angelina Co. Clinic, Clinic Bldg. Free; all venereal diseases.

Maud, Bowie Co.: Maud Clinic. Free; all venereal diseases.

McAllen, Hidalgo Co.: McAllen Clinic, Clinic Bldg., Main St. Free; all venereal diseases.

McKinney, Collin Co.: Collin Co. Clinic, City Hall. Free; all venereal diseases.

Midland, Midland Co.: Midland Co. Clinic, Courthouse. Free; all venereal diseases.

New Boston, Bowie Co.: New Boston Clinic. Free; all venereal diseases.

Pampa, Gray Co.: Pampa Clinic, City Hall. Free; all venereal diseases.

Port Arthur, Jefferson Co.: Port Arthur Clinic, City Hall. Free; all venereal diseases.

Port Isabel, Cameron Co.: Port Isabel Clinic, Dr. Hockaday's Office. Free; all venereal diseases.

Raymondville, Willacy Co.: Clinic, Clinic Building, % Dr. Conley. Free; all venereal diseases.

Sabinal, Uvalde Co.: Sabinal Clinic. Free; all venereal diseases.

San Angelo, Tom Green Co.: San Angelo Clinic, City Hall. Free; all venereal diseases.

San Antonio, Bexar Co.

San Antonio Clinic, 102 Dwyer Ave. Free; all venereal diseases.

Venereal Disease Clinic, Robert B. Green Hospital. Free; all venereal diseases.

San Augustine, San Augustine Co.: San Augustine Clinic, Courthouse. Free; all venereal diseases.

San Benito, Cameron Co.: San Benito Clinic, Health Unit Bldg. Free; all venereal diseases.

San Elizario, El Paso Co.: San Elizario Clinic. Free; all venereal diseases.

Shamrock, Wheeler Co.: Shamrock Clinic. Free; all venereal diseases.

Sims, Bowie Co.: Sims Clinic. Free; all venereal diseases.

Socorro, El Paso Co.: Socorro Clinic. Free; all venereal diseases.

Texarkana, Bowie Co.: Texarkana Clinic, Old Federal Bldg. Free; all venereal diseases.

Tyler, Smith Co.: Tyler-Smith Clinic, Courthouse. Free; all venereal diseases.

Uvalde, Uvalde Co.: Uvalde Co. Clinic, Health Center Bldg. Free; all venereal diseases.

Waco, McLennon Co.: City Hospital Venereal Disease Clinic. Free; all venereal diseases.

Waxahachie, Ellis Co.: Waxahachie Clinic, 200 North Jackson St. Free; all venereal diseases.

Weslaco, Hidalgo Co.: Weslaco Clinic. Free; all venereal diseases.

Wheeler, Wheeler Co.: Wheeler Co. Clinic, Wheeler Hospital. Free; all venereal diseases.

Wichita Falls, Wichita Co.: Wichita Falls Clinic, City Auditorium. Free; all venereal diseases.

Woodville, Tyler Co.: Hardin-Tyler Clinic, Courthouse. Free; all venereal diseases.

UTAH

Ogden, Weber Co.: Ogden Clinic, City and County Bldg. Free; all venereal diseases.

Salt Lake City, Salt Lake Co.: Salt Lake Co. Clinic, Twenty-first South and State Sts. Free; all venereal diseases.

VERMONT

Burlington, Chittenden Co.: Burlington Free Dispensary, University of Vermont Medical School. Free; all venereal diseases.

NOTE.—The venereal disease control program of Vermont is based on a plan of payments made to private physicians for the treatment of venereal diseases in indigent patients. While only one clinic is functioning, the addresses of physicians giving treatment for venereal diseases under the State plan may be obtained from State, county, and municipal health officers.

VIRGINIA

Abingdon, Washington Co.: Abingdon Clinic, Washington Co. Health Dept. Free; all venereal diseases.

Alexandria, Fairfax Co.:

Community Health Center, 218 South Columbus St. Part-pay; all venereal diseases.

Woodlawn Clinic, Woodlawn Clinic Bldg., F. D. R. 1. Free; all venereal diseases.

Altavista, Campbell Co.: Altavista Clinic, Municipal Bldg. Free; syphilis only.

Alton, Halifax Co.: Alton Clinic. Free; all venereal diseases.

Amherst, Amherst Co.: Amherst Co. Clinic. Free; all venereal diseases.

Appalachia, Wise Co.: Appalachia V. D. Clinic. Free; syphilis only.

Arlington, Arlington Co.:

Clarendon Clinic, Health Department, 1119 N. Hudson St. Free; syphilis only.

Virginia Highlands Clinic, Health Department, 506 South 23d St. Free; syphilis only.

Cherrydale Clinic, 4006 Lee Highway. Free; syphilis only.

Arvonia, Buckingham Co.: Arvonia Clinic. Free; all venereal diseases.

Ashland, Hanover Co.: Ashland Venereal Disease Clinic. Free; all venereal diseases.

Beaver Dam, Hanover Co.: Montpelier Clinic. Free; all venereal diseases.

Berryville, Clarke Co.: Berryville Clinic. Free; syphilis only.

Blacksburg, Montgomery Co.: Blacksburg Clinic.

Blackstone, Nottoway Co.: Blackstone Clinic, Power Building, Main St. Free; all venereal diseases.

Bluefield, Tazewell Co.: Bluefield Clinic. Free; syphilis only.

Bristol, Washington Co.: Bristol Clinic, Kings Mountain Memorial Hospital. Free; all venereal diseases.

Buckingham, Buckingham Co.: Buckingham Co. Clinic, Buckingham Courthouse. Free; all venereal diseases.

Burkeville, Nottoway Co.: Burkeville Clinic, Municipal Building. Free; all venereal diseases.

Cape Charles, Northampton Co.: Cape Charles Clinic, Times Building. Free; syphilis only.

Charlotte Courthouse, Charlotte Co.: Charlotte Co. Clinic. Free; syphilis only.

Charlottesville, Albemarle Co.:

Charlottesville Clinic, City Hall, Joint Health Department. Free; all venereal diseases.

University of Virginia V. D. Clinic, University of Virginia Hospital. Free; all venereal diseases.

Chase City, Mecklenburg Co.: Chase City Clinic, Chase City Department Store Bldg. Free; syphilis only.

Chatham, Pittsylvania Co.: Chatham Clinic. Free; all venereal diseases.

Christiansburg, Montgomery Co.: Christiansburg Venereal Disease Clinic. Free; all venereal diseases.

Clarksville, Mecklenburg Co.: Clarksville Clinic. Free; syphilis only.

Clintwood, Dickenson Co.: Clintwood Clinic. Free; syphilis only.

Covington, Alleghany Co.: Covington Clinic. Free; syphilis only.

Cumberland, Cumberland Co.: Cumberland Co. Clinic. Free and pay; all venereal diseases.

Danville, Pittsylvania Co.:
Danville Clinic, Municipal Building. Free; syphilis only; gonorrhea to limited extent.
Health Department Clinic. Free; syphilis only.

Denbigh, Warwick Co.: Denbigh Clinic, Health Department. Free; all venereal diseases.

Disputanta, Prince George Co.: Disputanta Clinic. Free; all venereal diseases.

Drivers, Nansemond Co.: Drivers Clinic, Health Department. Free; all venereal diseases.

Eastville, Northampton Co.: Eastville Clinic, Courthouse. Free; syphilis only.

Ellerson, Hanover Co.: Ellerson Clinic, Health Department. Free; all venereal diseases.

Emporia, Greenville Co.: Emporia Venereal Disease Clinic, Courthouse. Free; syphilis only.

Fairfax, Fairfax Co.: Fairfax Co. Clinic, Courthouse. Free; all venereal diseases.

Falls Church, Fairfax Co.: Falls Church Clinic, Odd Fellow's Hall. Free; all venereal diseases.

Farmville, Prince Edward Co.: Farmville Clinic, Southside Community Hospital. Pay; all venereal diseases.

Fincastle, Botetourt Co.: Fincastle Clinic, Fincastle Health Office. Free; syphilis only.

Franklin, Southampton Co.: Franklin Venereal Disease Clinic, Health Department. Free; syphilis only.

Fredericksburg, Spotsylvania Co.: City Clinic. Part-pay; syphilis only.

Front Royal, Warren Co.: Front Royal Venereal Disease Clinic, Courthouse. Free; all venereal diseases.

Gretna, Pittsylvania Co.: Gretna Venereal Disease Clinic. Free; all venereal diseases.

Grundy, Buchanan Co.: Grundy Clinic. Free; all venereal diseases.

Hampton, Elizabeth City Co.: Hampton Venereal Disease Clinic, Dixie Hospital. Free; all venereal diseases.

Harrisonburg, Rockingham Co.: Harrisonburg Venereal Disease Clinic, 234 East Market St. Free; syphilis only.

Herndon, Fairfax Co.: Herndon Clinic, Municipal Building. Free; all venereal diseases.

Hopewell, Prince George Co.: Hopewell Health Department, 200 North 9th St. Part-pay; all venereal diseases.

Hurley, Buchanan Co.: Hurley Clinic. Free; all venereal diseases.

Lawrenceville, Brunswick Co.: Lawrenceville Venereal Disease Clinic, Courthouse. Free; syphilis only.

Lebanon, Russell Co.: Lebanon Clinic. Free; syphilis only.

Lexington, Rockbridge Co.: Lexington Venereal Disease Clinic, Jackson Memorial Hospital. Free; all venereal diseases.

Luray, Page Co.: Luray Venereal Disease Clinic, Health Office. Free; all venereal diseases.

Lynchburg, Campbell Co.: Lynchburg Venereal Disease Clinic, 10th and Church Sts. Free; all venereal diseases.

Madison Heights, Amherst Co.: Madison Heights Clinic. Free; all venereal diseases.

Manassas, Prince William Co.: Manassas Clinic. Free; syphilis only.

Marion, Smyth Co.: Marion Venereal Disease Clinic, Smyth Co. Health Department. Free; syphilis only.

Martinsville, Henry Co.: Martinsville-Henry Co. Venereal Disease Clinic. Part-pay; syphilis only.

Mathews, Mathews Co.: Mathews Co. Venereal Disease Clinic. Part-pay; all venereal diseases.

Middleburg, Loudoun Co.: Middleburg Health Center, Madison St. Part-pay; all venereal diseases.

Nassawadox, Northampton Co.: Nassawadox Clinic, Memorial Hospital. Free; syphilis only.

Newport News, Warwick Co.:

Health Department Venereal Disease Clinic, 2516 Washington St. Free; all venereal diseases.

Peninsula Antisyphilitic Clinic, Wittaker Memorial Hospital, 1014 29th St. Free; all venereal diseases.

Norfolk, Norfolk Co.:

Community Hospital Venereal Disease Clinic, Corprew Ave. Free; all venereal diseases.

The Kings Daughters Clinic, 300 West York St. Free; all venereal diseases.

Norfolk Co. Medical Society Venereal Disease Clinic, Norfolk City Health Department. Free; all venereal diseases.

Public Clinic, 449 East Bute St. (Negro only.) Free or part-pay; all venereal diseases.

Norton, Wise Co.: Norton Clinic. Free; syphilis only.

Orange, Orange Co.: Orange Co. Venereal Disease Clinic, Main St. Free; all venereal diseases.

Petersburg, Dinwiddie Co.: Health Center, 14–16 North Market St. Part-pay and pay; all venereal diseases.

Portsmouth, Norfolk Co.: American Legion Clinic, New Market Building. Free; all venereal diseases.

Portsmouth, Norfolk Co.: Portsmouth Public Venereal Disease Clinic, 401 South Green St. Free and part-pay; syphilis only.

Princess Anne, Princess Anne Co.: Princess Anne Co. Venereal Clinic, Courthouse. Free; syphilis only.

Pulaski, Pulaski Co.: Pulaski Co. Venereal Clinic, 93 Second St., NW. Free; all venereal diseases.

Radford, Montgomery Co.: Radford Venereal Disease Clinic. Free; syphilis only.

Richlands, Tazewell Co.: Richlands Clinic. Free; syphilis only.

Richmond, Henrico Co.:

Church Hill Venereal Disease Clinic, 605 North 24th St. Free; syphilis only.

Community Clinic, 2 West Marshall St. Free and part-pay; syphilis only.

Medical College of Virginia Venereal Disease Clinic, 1201 East Marshall St. Part-pay; all venereal diseases.

West Cary Clinic, 1106–A West Cary St. Free; syphilis only.

Ringgold, Pittsylvania Co.: Taylorsville Clinic, Route 1. Free; all venereal diseases.

Roanoke, Roanoke Co.: Roanoke City Venereal Disease Clinic, 209 Church Ave., SW. Free; all venereal diseases.

Salem, Roanoke Co.:

Community Venereal Disease Clinic, 9 College Ave. Free; all venereal diseases.

Mercy House Clinic. Free; all venereal diseases.

South Boston, Halifax Co.: South Boston Venereal Disease Clinic. Free; all venereal diseases.

South Hill, Mecklenburg Co.: South Hill Venereal Disease Clinic, Old Masonic Hall. Part-pay; syphilis only.

Staunton, Augusta Co.: Staunton Venereal Disease Clinic, 10 East Johnson St. Free; syphilis only.

Stony Creek, Sussex Co.: Stony Creek Clinic, Health Office Building. Free; all venereal diseases.

St. Paul, Wise Co.: St. Paul Clinic. Free; syphilis only.

Suffolk, Nansemond Co.: Suffolk Clinic, Health Department. Free; all venereal diseases.

Tappahannock, Essex Co.: Essex Co. Clinic. Part-pay; syphilis only.

Toano, James City Co.: Toano Venereal Disease Clinic, Health Department. Free; syphilis only.

Urbanna, Middlesex Co.: Middlesex Co. Clinic. Free; syphilis only.

Vinton, Roanoke Co.: Vinton Community Welfare, Municipal Building. Free; all venereal diseases.

Virginia Beach, Princess Anne Co.: Virginia Beach Clinic. Free; all venereal diseases.

Wakefield, Sussex Co.: Wakefield Clinic, Town Hall. Free; all venereal diseases.

Waverly, Sussex Co.: Waverly Clinic, Main St. Free; all venereal diseases.

Waynesboro, Augusta Co.: Waynesboro Venereal Diseases Clinic, City Hall Annex. Free; syphilis only.

Williamsburg, James City Co.: Williamsburg Venereal Diseases Clinic, Health Department. Free; all venereal diseases.

Woodstock, Shenandoah Co.: Woodstock Venereal Diseases Clinic, Health Office. Free; all venereal diseases.

Wytheville, Wythe Co.: Wytheville Venereal Disease Clinic, Main St. Free; syphilis only.

Yorktown, York Co.: Yorktown Clinic. Free; all venereal diseases.

WASHINGTON

Aberdeen, Grays Harbor Co.: Public Health Clinic, Aberdeen General Hospital. Free; all venereal diseases.

Bellingham, Whatcom Co.: Public Health Clinic, Courthouse, G St. Free; all venereal diseases.

Centralia, Lewis Co.: Office of Dr. O. C. Kroger. Free; all venereal diseases.

Colfax, Whitman Co.: Whitman Co. Health Department, Grady Building. Free; all venereal diseases.

Everett, Snohomish Co.: Snohomish Co. Health Department, County Building. Free; all venereal diseases.

Grand Coulee, Grant Co.: Grand Coulee Clinic. Free; all venereal diseases.

Kelso, Cowlitz Co.: Cowlitz Co. Clinic, Courthouse. Free; all venereal diseases.

Olympia, Thurston Co.: Thurston Co. Clinic, Courthouse. Free; all venereal diseases.

Port Angeles, Clallam Co.: County-City Health Department Clinic, Courthouse. Free; all venereal diseases.

Seattle, King Co.:

Health Department Clinic, 416 Yesler Way. Free and part-pay; all venereal diseases.

King Co. Clinic, Hospital System, 325 Ninth Ave. Free; all venereal diseases.

Spokane, Spokane Co.: City Health Department Clinic, City Hall. Free; all venereal diseases.

Tacoma, Pierce Co.: Tacoma Public Health Clinic, 322 Provident Building. Free and part-pay; all venereal diseases.

Vancouver, Clark Co.: City Health Department, Municipal Building. Free; all venereal diseases.

Walla Walla, Walla Walla Co.: City-County Clinic, Courthouse. Free; all venereal diseases.

Wenatchee, Chelan Co.: Chelan Co. Clinic, Courthouse Building. Free; all venereal diseases.

Yakima, Yakima Co.: Yakima Co. Health Department, City Hall. Free; syphilis and gonorrhea only.

WEST VIRGINIA

Beckley, Raleigh Co.: Raleigh Co. Venereal Disease Clinic. Free; all venereal diseases.

Berkeley Springs, Morgan Co.: Venereal Disease Clinic. Free; all venereal diseases.

Bluefield, Mercer Co.: Bluefield Venereal Disease Clinic, Municipal Bldg. Free; all venereal diseases.

Buckhannon, Upshur Co.: Upshur Co. Venereal Disease Clinic. Free; all venereal diseases.

Charleston, Kanawha Co.:

Charleston Clinic, City Bldg. Free; all venereal diseases.

Kanawha Co. Venereal Clinic, Courthouse. Free; syphilis only.

Charles Town, Jefferson Co.: Jefferson Co. Venereal Clinic. Free; all venereal diseases.

Clarksburg, Harrison Co.: City-County Clinic, Courthouse. Free; all venereal diseases.

Clay, Clay Co.: Clay Co. Venereal Disease Clinic. Free; all venereal diseases.

East Rainelle, Greenbrier Co.: Greenbrier Co. Venereal Disease Clinic. Free; all venereal diseases.

Elkins, Randolph Co.: D. P. A. Clinic. Free; all venereal diseases.

Fairmont, Marion Co.: Marion Co. Health Department, Venereal Diseases. Free; all venereal diseases.

Fayetteville, Fayette Co.: Fayette Co. Venereal Disease Clinic. Free; all venereal diseases.

Glenville, Gilmer Co.: Gilmer Co. Venereal Disease Clinic. Free; all venereal diseases.

Grafton, Taylor Co.: Taylor Co. Clinic, Grafton City Hospital. Free; all venereal diseases.

Grantsville, Calhoun Co.: Calhoun Co. Clinic. Free; all venereal diseases.

Hamlin, Lincoln Co.: Lincoln Co. Venereal Disease Clinic. Free; all venereal diseases.

Harrisville, Ritchie Co.: Ritchie Co. Venereal Disease Clinic. Free; all venereal diseases.

Hinton, Summers Co.: Summers Co. Venereal Disease Clinic, Rose Building. Free; all venereal diseases.

Huntington, Cabell Co.: City Clinic, City Building. Free and part-pay; all venereal diseases.

Keyser, Mineral Co.: Mineral Co. Venereal Clinic. Free; syphilis and gonorrhea only.

Kingswood, Preston Co.: Preston Co. Clinic. Free; all venereal diseases.

Lewisburg, Greenbrier Co.: Greenbrier Co. Venereal Disease Clinic. Free; all venereal diseases.

Logan, Logan Co.: Logan Co. Clinic, Basement of Courthouse. Free; all venereal diseases.

Man, Logan Co.: Man V. D. Clinic. Free; syphilis only.

Madison, Boone Co.: Boone Co. Health Department, Madison Clinic. Free; all venereal diseases.

Marlinton, Pocahontas Co.: Pocahontas Co. Venereal Disease Clinic, Courthouse. Free; all venereal diseases.

Martinsburg, Berkeley Co.: Berkeley Co. Clinic, County Courthouse. Free; all venereal diseases.

Montgomery, Fayette Co.: Fayette Co. V. D. Clinic. Free; all venereal diseases.

Morgantown, Monongalia Co.: Monongalia Co. Venereal Disease Clinic, 224 Kirk St. Free; all venereal diseases.

Moundsville, Marshall Co.: Marshall Co. Health Department, 315 Jefferson Ave. Free; all venereal diseases.

Mullens, Wyoming Co.: Wyoming Co. Health Department. Free; all venereal diseases.

New Cumberland, Hancock Co.: Hancock Co. Health Department. Free; all venereal diseases.

New Martinsville, Wetzel Co.: Wetzel Co. Health Department. Free; all venereal diseases.

Omar, Logan Co.: Omar Clinic, Basement of Courthouse. Free; syphilis only.

Parkersburg, Wood Co.: Wood Co. Venereal Disease Clinic, City Bldg. Annex. Free; all venereal diseases.

Parsons, Tucker Co.: Tucker Co. Venereal Disease Clinic. Free; all venereal diseases.

Petersburg, Grant Co.: Hardy-Grant-Pendelton Clinic, Care of Public Health Nurse. Free; all venereal diseases.

Philippi, Barbour Co.: Barbour Co. Venereal Disease Clinic. Free; all venereal diseases.

Point Pleasant, Mason Co.: Mason Co. Venereal Disease Clinic, 221 Sixth St. Free; all venereal diseases.

Princeton, Mercer Co.: Mercer Co. Venereal Disease Clinic, Courthouse. Free; all venereal diseases.

Richwood, Nicholas Co.: Richwood Clinic, Cor. Oakford and Main Sts. (White only.) Free; all venereal diseases.

Romney, Hampshire Co.: Hampshire Co. Clinic. Free; all venereal diseases.

Shepherdstown, Jefferson Co.: Shepherdstown Clinic. Free; all venereal diseases.

Spencer, Roane Co.: Roane Co. Venereal Disease Clinic, Church St. Free; all venereal diseases.

Summersville, Nicholas Co.: Summersville Clinic. (White only.) Free; all venereal diseases.

Sutton, Braxton Co.: Braxton Co. Venereal Disease Clinic. Free; all venereal diseases.

Union, Monroe Co.: Monroe Co. Clinic. Free; all venereal diseases.

Wayne, Wayne Co.: Wayne Co. Venereal Disease Clinic. Free; all venereal diseases.

Webster Springs, Webster Co.: Webster Co. Health Department. (Negro only.) Free; all venereal diseases.

Weirton, Hancock Co.: Weirton Christian Center, County Health Department. Free; all venereal diseases.

Welch, McDowell Co.: McDowell Co. Venereal Disease Clinic. Free; all venereal diseases.

Wellsburg, Brooke Co.: Brooke Co. Health Department. Free; all venereal diseases.

Weston, Lewis Co.: Lewis Co. Venereal Disease Clinic, Tierney Building, Main Ave. Free; all venereal diseases.

West Union, Doddridge Co.: Doddridge Co. Venereal Disease Clinic, Columbia. (White only.) Free; all venereal diseases.

Wheeling, Ohio Co.: City-County Health Department. Free; all venereal diseases.

Whitesville, Boone Co.: Boone Co. Health Department. Free; all venereal diseases.

Williamson, Mingo Co.: Mingo Co. Venereal Disease Clinic. Free; syphilis only.

Winfield, Putnam Co.: Putnam Co. Venereal Disease Clinic, County Health Department. Free; all venereal diseases.

WISCONSIN

Beloit, Rock Co.: City Health Clinic, City Health Department. Free; all venereal diseases.

Green Bay, Brown Co.: City Health Clinic, 523 Howe St. Free; all venereal diseases.

Janesville, Rock Co.: State Clinic, City Hall. Free; all venereal diseases.

Kenosha, Kenosha Co.: State Clinic, City Hall. Free; all venereal diseases.

La Crosse, La Crosse Co.: State Clinic, City Health Department, City Hall. Free; all venereal diseases.

Madison, Dane Co.: State Clinic, 112 North Hamilton St. Free; all venereal diseases.

Milwaukee, Milwaukee Co.:

City Health Department Clinic, City Hall. Free; all venereal diseases.

County Dispensary, 2430 West Wisconsin Ave. Free; syphilis only.

Mt. Sinai Clinic, 908 North Twelfth St. Part-pay; all venereal diseases.

Night Clinic, City Hall. Free; syphilis only.

Urban League, 904 West Vine St. (Negro only.) Free; all venereal diseases.

Oshkosh, Winnebago Co.: State Clinic, 28½ State St. Free; all venereal diseases.

Racine, Racine Co.: City Health Clinic, City Hall. Free; all venereal diseases.

Superior, Douglas Co.: State Clinic, 1323 Broadway. Free; all venereal diseases.

Wausau, Marathon Co.: State Clinic, 314½ Scott St. Free; all venereal diseases.

Waukesha, Waukesha Co.: State Clinic, Waukesha Memorial Hospital. Free; syphilis only.

WYOMING

Casper, Natrona Co.: Casper Clinic, Memorial Hospital. Free; all venereal diseases.

Cheyenne, Laramie Co.: Cheyenne Clinic, Memorial Hospital. Free; all venereal diseases.

Rock Springs, Sweetwater Co.: Rock Springs Clinic, General Hospital. Free; all venereal diseases.

Directory of Clinics

FOR THE DIAGNOSIS AND TREATMENT OF VENEREAL DISEASES

Supplement No. 4 to Venereal Disease Information

Revised 1942

FS 2.10

FEDERAL SECURITY AGENCY

PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

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This directory is for the information of health officers, physicians, nurses, and social workers in referring persons unable to pay for private care to public or semipublic medical agencies for the diagnosis and treatment of the venereal diseases.

The directory is recommended for use in clinics as an aid in the transfer of patients and in agencies whose clients may be in need of medical care for the venereal diseases.

The listing is by State and municipality. The name and address of the clinic is given with information on the types of patients who are eligible for treatment on the cost of treatment, and on the disease treated.

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
	ALABAMA						
ABBEVILLE HENRY CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
ADA MONTGOMERY COUNTY	COUNTY V D CLINIC	ALL	✓	✓	✓		
ALBERTVILLE MARSHALL CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
ALEXANDER CITY TALLAPOOSA CO	COUNTY CLINIC MASONIC HALL	ALL	✓	✓	✓		
ALICEVILLE PICKENS CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
ANUALUSIA COVINGTON CO	COUNTY CLINIC COUNTY HEALTH UNIT	ALL	✓	✓	✓		
ANNISTON CALHOUN CO	COUNTY CLINIC CO COURTHOUSE ANNEX	ALL	✓	✓	✓		
ASHLAND CLAY CO	COUNTY CLINIC COURTHOUSE ANNEX	ALL	✓	✓	✓		
ASHVILLE ST CLAIR CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
ATHENS LIMESTONE CO	COUNTY CLINIC BROWNS FERRY ST	ALL	✓	✓	✓		
ATMORE ESCAMBIA CO	COUNTY CLINIC BANK OF ATMORE BLDG	ALL	✓	✓	✓		
AUBURN LEE CO	COUNTY CLINIC OPELIKA ROAD	ALL	✓	✓	✓		
AUTAUGAVILLE AUTAUGA CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
BAY MINETTE BALOWIN CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
BAYOU LABATRE MOBILE CO	COUNTY CLINIC DR TAPIAS OFFICE	ALL	✓	✓	✓		
BEATRICE MONROE CO	V O CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
BELMONT SUMTER CO	COUNTY V D CLINIC BRANCH HEALTH OFFICE	ALL	✓	✓	✓		
BESSEMER JEFFERSON CO	COUNTY CLINIC 1724 THIRD AVENUE N	ALL	✓	✓	✓	✓	
BIRDINE GREENE CO	GREENE CO MOBILE TOWN CHURCH	ALL	✓	✓	✓		
BIRMINGHAM JEFFERSON CO	EASTERN H CENTER 8 NO 59TH ST	ALL	✓	✓	✓		
BIRMINGHAM JEFFERSON CO	HILLMAN HOSPITAL 620 SOUTH 20TH ST	ALL	✓	✓	✓	✓	✓
BIRMINGHAM JEFFERSON CO	SLOSSFIELD CLINIC 2501 19TH ST N	N	✓	✓	✓		
BIRMINGHAM JEFFERSON CO	WESTERN H CENTER 2215 ENSLEY AVE	ALL	✓	✓	✓		

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ALABAMA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
BLEECKER LEE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
BOLIGEE GREENE CO	GREENE CO MOBILE DR TRICES OFFICE	ALL	✓	✓	✓		
BREWTON ESCAMBIA CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
BUTLER CHOCTAW CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
CAMDEN WILCOX CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
CARROLLTON PICKENS CO	COUNTY CLINIC HILL DRUG STORE	ALL	✓	✓	✓		
CENTER CHEROKEE CO	CO HEALTH OFFICE COURTHOUSE	ALL	✓	✓	✓		
CENTERVILLE BIBB CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
CHAPMAN BUTLER CO	V D CLINIC DR J C JOHNSTONS OFC	ALL	✓	✓	✓		
CHATOM WASHINGTON CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
CHEROKEE COLBERT CO	V D CLINIC BRANCH HEALTH OFFICE	ALL	✓	✓	✓		
CHILDERSBURG TALLADEGA CO	COUNTY CLINIC DR R P STOCKS OFFICE	ALL	✓	✓	✓		
CITRONELLE MOBILE CO	COUNTY CLINIC DR THOMPSONS OFFICE	ALL	✓	✓	✓		
CLANTON CHILTON CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
COFFEEVILLE CLARKE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
COLUMBIANA SHELBY CO	COUNTY CLINIC MAIN ST	ALL	✓	✓	✓		
COURTLAND LAWRENCE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
CULLMAN CULLMAN CO	COUNTY CLINIC CULLMAN HOSPITAL	ALL	✓	✓	✓		
DADEVILLE TALLAPOOSA CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
DECATUR MORGAN CO	COUNTY CLINIC 302 SECOND AVE	ALL	✓	✓	✓		
DEMOPOLIS MARENGO CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
DOTHAN HOUSTON CO	COUNTY CLINIC 117 NORTH ST	ALL	✓	✓	✓		
DOUBLE SPRINGS WINSTON CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
ELBA COFFEE CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
ENTERPRISE COFFEE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
EOFALA BARBOUR CO	COUNTY V O CLINIC BRANCH HEALTH OFFICE	ALL	✓	✓	✓		
EUTAW GREENE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
EVERGREEN CONECUH CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
FAIRFAX CHAMBERS CO	COUNTY CLINIC COL HEALTH CENTER	ALL	✓	✓	✓		
FAIRHOPE BALDWIN CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
FAYETTE FAYETTE CO	COUNTY CLINIC NORTH PEYTON ST	ALL	✓	✓	✓		
FLORALA COVINGTON CO	V O CLINIC DR GALLOWAYS OFFICE	ALL	✓	✓	✓		
FLORENCE LAUDERDALE CO	COUNTY CLINIC COURT AND TENN STS	ALL	✓	✓	✓		
FORKLAND GREENE CO	GREENE CO MOBILE MIUULE OF TOWN	ALL	✓	✓	✓		
FORT PAYNE DEKALB CO	COUNTY CLINIC CO ACTIVITIES BLDG	ALL	✓	✓	✓		
FRUITDALE WASHINGTON CO	V O CLINIC BRANCH HEALTH OFFICE	ALL	✓	✓	✓		
FRUITDALE WASHINGTON CO	COUNTY CLINIC	ALL	✓	✓	✓		
GEIGER SUMTER CO	COUNTY V O CLINIC BRANCH HEALTH OFFICE	ALL	✓	✓	✓		
GENEVA GENEVA CO	COUNTY CLINIC ACADEMY ST	ALL	✓	✓	✓		
GEORGIANA BUTLER CO	COUNTY CLINIC FIRST NATL BANK BLDG	ALL	✓	✓	✓		
GOOD WATER COOSA CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
GOROO PICKENS CO	V O CLINIC CITY HALL	ALL	✓	✓	✓		
GREENSBORO HALE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
GREENVILLE BUTLER CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
GROVE HILL CLARKE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
HALEYVILLE WINSTON CO	COUNTY CLINIC CITY HALL MAIN ST	ALL	✓	✓	✓		
HAMILTON MARION CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
HAYNEVILLE LOWNDES CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
HEADLAND HENRY CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
HEFLIN CLEBURNE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		

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ALABAMA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
HOBSON CITY CALHOUN CO	V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
HUNTSVILLE MADISON CO	COUNTY CLINIC COURTHOUSE ANNEX	ALL	✓	✓	✓		
HURTSBORO RUSSELL CO	V D CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
JACKSONVILLE CALHOUN CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
JASPER WALKER CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
LANETT CHAMBERS CO	COUNTY CLINIC GOODSELL M E CHURCH	ALL	✓	✓	✓		
LEIGHTON COLBERT CO	COUNTY CLINIC OVER MODEL DRUGSTORE	ALL	✓	✓	✓		
LINDEN MARENGO CO	V D CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
LINEVILLE CLAY CO	V D CLINIC YOUNGS DRUG STORE	ALL	✓	✓	✓		
LIVINGSTON SUMTER CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
LOACHAPOKA LEE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
LUVERNE CRENSHAW CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
MANTUA GREENE CO	GREENE CO MOBILE MR EATMANS STORE	ALL	✓	✓	✓		
MAPLESVILLE CHILTON CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
MARION PERRY CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
MIDWAY BULLOCK CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
MILLPORT LAMAR CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
MINTER DALLAS CO	V D CLINIC RICHMOND TR SCHOOL	ALL	✓	✓	✓		
MOBILE MOBILE CO	COUNTY CLINIC CITY HOSPITAL	ALL	✓	✓	✓		
MONROEVILLE MONROE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
MONTEVALLO SHELBY CO	COUNTY CLINIC FANCHER BLDG MAIN ST	ALL	✓	✓	✓		
MONTGOMERY MONTGOMERY CO	FRATERNAL HOSPITAL 42 DORSEY ST	N	✓		✓		
MONTGOMERY MONTGOMERY CO	CITY ARMORY CL DIXIE GRAVES FORT	ALL	✓		✓		
MONTGOMERY MONTGOMERY CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
MONTGOMERY MONTGOMERY CO	V D CLINIC STATE TEACHERS COL	N	✓		✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
MOULTON LAWRENCE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
MOUNDVILLE HALE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
MT VERNON MOBILE CO	COUNTY CLINIC DR TISDALES OFFICE	ALL	✓	✓	✓		
MULBERRY AUTAUGA CO	MULBERRY CLINIC UNDERWOOD BLDG	ALL	✓	✓	✓		
NEW BROCKTON COFFEE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
ONEONTA BLOUNT CO	COUNTY CLINIC CO ACTIVITIES BLDG	ALL	✓	✓	✓		
OPELIKA LEE CO	COUNTY CLINIC 9TH ST AND SO RR AVE	ALL	✓	✓	✓		
OPELIKA LEE CO	MARVYN CLINIC ROUTE 2	ALL	✓	✓	✓		
OPP COVINGTON CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
ORRVILLE DALLAS CO	V D CLINIC BRANCH HEALTH OFFICE	ALL	✓	✓	✓		
OZARK DALE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
PELL CITY ST CLAIR CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
PHENIX CITY RUSSELL CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
PITTSVIEW RUSSELL CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
PLEASANT RIDGE GREENE CO	GREENE CO MOBILE STEELES STORE	ALL	✓	✓	✓		
PRATTVILLE AUTAUGA CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
PRICHARD MOBILE CO	COUNTY CLINIC CITY HALL ANNEX	ALL	✓	✓	✓		
RAGLAND ST CLAIR CO	COUNTY CLINIC CORBINS DRUG STORE	ALL	✓	✓	✓		
REFORM PICKENS CO	V D CLINIC WIMBERLY BUILDING	ALL	✓	✓	✓		
REPTON CONECUH CO	COUNTY CLINIC OLD POST OFFICE BLDG	ALL	✓	✓	✓		
ROANOKE RANDOLPH CO	COUNTY CLINIC BRANCH HEALTH OFFICE	ALL	✓	✓	✓		
ROCKFORD COOSA CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
RUSSELLVILLE FRANKLIN CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
ST CLAIRE LOUNDES CO	V D CLINIC GENERAL STORE	ALL	✓	✓	✓		
SCOTTSBORO JACKSON CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		

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ALABAMA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
SEALE RUSSELL CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
SELMA DALLAS CO	COUNTY CLINIC 109 CHURCH ST	ALL	✓	✓	✓		
SHEFFIELD COLBERT CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
SIMSVILLE BULLOCK CO	COUNTY V D CLINIC OR GUTHRIES OFFICE	ALL	✓	✓	✓		
SPRINGVILLE ST CLAIR CO	COUNTY CLINIC DR GRASBERGERS OFC	ALL	✓	✓	✓		
STEVENSON JACKSON CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
SULLIGENT LAMAR CO	COUNTY CLINIC ELM ST	ALL	✓	✓	✓		
SWEET WATER MARENGO CO	V D CLINIC BRANCH HEALTH OFFICE	ALL	✓	✓	✓		
SYLACAUGA TALLADEGA CO	COUNTY CLINIC 3RD AND NORTON STS	ALL	✓	✓	✓		
TALLADEGA TALLADEGA CO	COUNTY CLINIC COURT AND SOUTH STS	ALL	✓	✓	✓		
TISHABEE GREENE CO	GREENE CO MOBILE SPRINGHILL CHURCH	ALL	✓	✓	✓		
TROY PIKE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
TUSCALOOSA TUSCALOOSA CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
TUSCUMBIA COLBERT CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
TUSKECEE MACON CO	MACON CO MOBILE ADAMS STORE	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE ARMSTRONG	ALL	✓	✓	✓		
TUSKECEE MACON CO	MACON CO MOBILE BROWNVILLE	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE CARRS STORE	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE CHESSON	ALL	✓	✓	✓		
TUSKECEE MACON CO	MACON CO MOBILE CREEK STAND	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE CROSS ROADS	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE DOWNS	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE FORT DAVIS	ALL	✓	✓	✓		
TUSKECEE MACON CO	MACON CO MOBILE HANNON	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE HADAWAY	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
TUSKEGEE MACON CO	MACON CO MOBILE JAMES STATION	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE LITTLE TEXAS	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE LIVERPOOL	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE LOG CABIN	ALL	✓	✓	✓		
TUSKEGEE MACON CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE MILSTEAD	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE MT ESTHER	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE MT NEBO	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE MT PLEASANT	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE MT ZION	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE PINKSTONS STORE	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE ROBA	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE ST PAUL	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE SEGREST	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE SHILOH	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE SOCIETY HILL	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE SWANSON	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE TYSONVILLE	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE VINE BETHEL	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE WARRIOR STANO	ALL	✓	✓	✓		
TUSKEGEE MACON CO	MACON CO MOBILE WHITE CHURCH	ALL	✓	✓	✓		
UNION SPRINGS BULLOCK CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
UNIONTOWN PERRY CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
URIAH MONROE CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
VINCENT SHELBY CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TD *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
WAOLEY RANUOLPH CO	V U CLINIC BRANCH HEALTH OFFICE	ALL	✓	✓	✓		
WAVERLY LEE CO	V O CLINIC UR COGGINS OFFICE	ALL	✓	✓	✓		
WEUOWEE RANUOLPH CO	COUNTY CLINIC COURTHOUSE	ALL	✓		✓		
WEST BLOCTON BIBB CO	COUNTY CLINIC BRANCH HEALTH OFFICE	ALL	✓	✓	✓		
WEST GREEN GREENE CO	GREENE CO MOBILE WILLIAMS STORE	ALL	✓	✓	✓		
WETUMPKA ELMORE CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
YORK SUMTER CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
	ARIZONA						
AJO PIMA CO	V O CLINIC	ALL	✓		✓		
BISBEE COCHISE CO	COUNTY HEALTH UNIT	ALL	✓		✓		
BUCKEYE MARICOPA CO	V U CLINIC	ALL	✓	✓	✓		
OOUGLAS COCHISE CO	COUNTY HEALTH UNIT	ALL	✓		✓		
FLAGSTAFF COCONINO CO	COUNTY HEALTH UNIT COUNTY COURT HOUSE	ALL	✓	✓	✓		
PHOENIX MARICOPA CO	COUNTY HEALTH UNIT 3 NORTH 17TH AVE	ALL	✓	✓	✓		–
PHOENIX MARICOPA CO	ST MONICA CLINIC 809 SOUTH 7TH AVE	N	✓		✓		
PHOENIX MARICOPA CO	SOC SERVICE CENTER 702 EAST AOAMS ST	W	✓	✓	✓		
PRESCOTT YAVAPAI CO	COUNTY CLINIC ROOM 2 BASHFORO BLUG	ALL	✓	✓	✓		
TUCSON PIMA CO	COUNTY V O CLINIC ROOM 14 COURTHOUSE	ALL	✓	✓	✓		
WINSLOW NAVAJO CO	COUNTY CLINIC MATERNITY HOME	ALL	✓		✓	✓	
YUMA YUMA CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓	✓	

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY	PAY
	ARKANSAS						
ARKADELPHIA CLARK CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓		✓		
ASHDOWN LITTLE RIVER CO	COUNTY CLINIC COURTHOUSE	ALL	✓		✓		
AUGUSTA WOODRUFF CO	COUNTY CLINIC COURTHOUSE	ALL	✓		✓		
BATESVILLE INDEPENDENCE CO	COUNTY HEALTH UNIT BARNETT BLDG MAIN ST	ALL	✓		✓		
BAUXITE SALINE CO	COUNTY HEALTH UNIT MEXICAN CAMP	ALL	✓	✓	✓		
BEARDON OUACHITA CO	V D CLINIC DOHERTYS DRUG STORE	ALL	✓	✓	✓		
BENTON SALINE CO	COUNTY HEALTH UNIT	ALL	✓	✓	✓		
BENTONVILLE BENTON CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
BLYTHEVILLE MISSISSIPPI CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓		✓		
CAMDEN OUACHITA CO	V D CLINIC COUNTY COURTHOUSE	ALL	✓	✓	✓		
CLARKSVILLE JOHNSON CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓		✓		
CONWAY FAULKNER CO	PALARM CLINIC COURTHOUSE	ALL	✓	✓	✓		
COTTON PLANT WOODRUFF CO	COUNTY HEALTH UNIT LEGION HUT	ALL	✓	✓	✓		
DARDANELLE YELL CO	COUNTY CLINIC COURT HOUSE	ALL	✓	✓	✓		
ELAINE PHILLIPS CO	PHILLIPS CO MOBILE OR KOLTGENS OFFICE	ALL	✓	✓	✓		
FAYETTEVILLE WASHINGTON CO	COUNTY CLINIC COURTHOUSE	ALL	✓		✓		
FORREST CITY ST FRANCIS CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓		✓		
FORT SMITH SEBASTIAN CO	COUNTY HEALTH UNIT WELFARE BLDG	ALL	✓	✓	✓		
GARLAND CITY MILLER CO	COUNTY HEALTH UNIT LOWES FARM	ALL	✓	✓	✓		
GOULD LINCOLN CO	COUNTY HEALTH UNIT ROUTE NO 1	ALL	✓	✓	✓		
GURDON CLARK CO	COUNTY HEALTH UNIT	ALL	✓		✓		
HAMBURG ASHLEY CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		
HARRISON BOONE CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		

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ARKANSAS

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
HELENA PHILLIPS CO	PHILLIPS CO MOBILE COURT HOUSE	ALL	✓	✓	✓		
HOPE HEMPSTEAD CO	COUNTY HEALTH UNIT COUHTHOUSE	ALL	✓		✓		
HOT SPRINGS GAHLAND CO	LEVI MEM HOSP CLINIC PROSPECT AVE	ALL	✓	✓	✓		
HOT SPRINGS GARLAND CO	U S P H S CLINIC SPRING ST	ALL	✓	✓	✓		
HUGHES ST FRANCIS CO	COUNTY HEALTH UNIT	ALL	✓		✓		
JONESBORO CRAIGHEAD CO	COUNTY HEALTH UNIT COUHTHOUSE	ALL	✓	✓	✓		
LAKE VIEW PHILLIPS CO	PHILLIPS CO MOBILE RESETTLEMENT	ALL	✓	✓	✓		
LITTLE ROCK PULASKI CO	CITY HEALTH DEPT CITY HALL	ALL	✓		✓		
LITTLE ROCK PULASKI CO	ISAAC FOLSOM CLINIC 12TH AND MCALMOT STS	ALL	✓	✓	✓		
LITTLE ROCK PULASKI CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		
LITTLE ROCK PULASKI CO	V GR BAUCUM CLINIC MEMPHIS HIGHWAY HT 1	ALL	✓	✓	✓		
MC GEHEE DESHA CO	COUNTY HEALTH UNIT	ALL	✓	✓	✓		
MALVERN HOT SPRINGS CO	COUNTY HEALTH UNIT	ALL	✓	✓	✓		
MARIANNA LEE CO	BRICKEYS CLINIC	ALL	✓	✓	✓		
MARIANNA LEE CO	LEE CO MOBILE CHESTNUT STREET	ALL	✓		✓		
MARIANNA LEE CO	LEE CO MOBILE POLK PLANTATION RT 1	ALL	✓		✓		
MAHIANNA LEE CO	PHAHR PLACE CLINIC	ALL	✓		✓		
MARIANNA LEE CO	WESTOR CLINIC 7 MI WEST MARIANNA	ALL	✓	✓	✓		
MAHION CRITTENDEN CO	COUNTY HEALTH UNIT	ALL	✓	✓	✓		
MARSHALL SEARCY CO	COUNTY HEALTH UNIT ADAMS BLDG	ALL	✓		✓		
MAHVELL PHILLIPS CO	PHILLIPS CO MOBILE	ALL	✓	✓	✓		
MELLWOOD PHILLIPS CO	PHILLIPS CO MOBILE POST OFFICE	ALL	✓	✓	✓		
MONTICELLO DREW CO	COUNTY HEALTH UNIT COUHTHOUSE	ALL	✓	✓	✓		
MORRILTON CONWAY CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		
NEWPORT JACKSON CO	COUNTY HEALTH UNIT COUHTHOUSE	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
NORTH LITTLE ROCK PULASKI CO	CITY CLINIC 116 EAST 3RD ST	ALL	✓	✓	✓		
OKOLONA CLARK CO	COUNTY HEALTH UNIT	ALL	✓		✓		
OSCEOLA MISSISSIPPI CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓		✓		
OZARK FRANKLIN CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓		✓		
PARIS LOGAN CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓		✓		
PINE BLUFF JEFFERSON CO	COUNTY HEALTH UNIT 6TH AND CHESTNUT	ALL	✓	✓	✓		
PINE BLUFF JEFFERSON CO	COUNTY HEALTH UNIT 214 NATIONAL BLDG	ALL	✓	✓	✓		
PRESCOTT NEVADA CO	COUNTY HEALTH UNIT CITY HALL	ALL	✓	✓	✓		
RISON CLEVELAND CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		
ROGERS BENTON CO	COUNTY HEALTH UNIT CITY HALL	ALL	✓	✓	✓		
RUSSELLVILLE POPE CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		
SEARCY WHITE CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		
SILOAM SPRINGS BENTON CO	COUNTY HEALTH UNIT LEGION HUT	ALL	✓	✓	✓		
SIMSBORO CRITTENDEN CO	COUNTY HEALTH UNIT	ALL	✓	✓	✓		
SNOW LAKE PHILLIPS CO	PHILLIPS CO MOBILE THORNTONS STORE	ALL	✓	✓	✓		
STAR CITY LINCOLN CO	COUNTY HEALTH UNIT	ALL	✓	✓	✓		
TEXARKANA MILLER CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		
TRENTON PHILLIPS CO	PHILLIPS CO MOBILE POST OFFICE	ALL	✓	✓	✓		
TUCKERMAN JACKSON CO	PHYSICANS OFFICE OR K K KIMBERLIN	ALL	✓	✓	✓		
VAN BUREN CRAWFORD CO	CO HEALTH DEPT COURTHOUSE	ALL	✓		✓		
WABASH PHILLIPS CO	PHILLIPS CO MOBILE HOWES STORE	ALL	✓	✓	✓		
WARREN BRADLEY CO	COUNTY HEALTH UNIT 200 MAIN ST	ALL	✓	✓	✓		
WEST MEMPHIS CRITTENDEN CO	COUNTY HEALTH UNIT	ALL	✓	✓	✓		
WILMOT ASHLEY CO	COUNTY HEALTH UNIT CITY HALL	ALL	✓	✓	✓		
WILSON MISSISSIPPI CO	V D CLINIC OFFICE OF DR ELLIS	ALL	✓		✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
WINCHESTER OREW CO	CO HEALTH UNIT HIGH SCHOOL	ALL	✓	✓	✓		
WINCHESTER OREW CO	V D CLINIC OSWALOS STORE	ALL	✓	✓	✓		
WYNNE CROSS CO	COONTY HEALTH UNIT	ALL	✓		✓		
YELLVILLE MARION CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		
	CALIFORNIA						
ALHAMBRA LOS ANGELES CO	HEALTH CENTER 612 WEST SHORB ST	ALL	✓	✓	✓		
ALTADENA LOS ANGELES CO	HEALTH CENTER 331 CROSBY ST	ALL	✓	✓	✓		
ARLINGTON RIVERSIDE CO	CO HOSPITAL CLINIC 9851 MAGNOLIA AVE	ALL	✓	✓	✓		
ARVIN KERN CO	V D CLINIC	ALL	✓	✓	✓		
ATASCADERO SAN LUIS OBISPO	ATASCADERO GEN HOSP	ALL	✓	✓	✓		
AZUSA LOS ANGELES CO	HEALTH CENTER 160 AZUSA ST	ALL	✓	✓	✓		
BAKERSFIELD KERN CO	KERN GENERAL HOSP 1800 FLOWER ST	ALL	✓	✓	✓		
BANNING RIVERSIDE CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
BARSTOW SAN BERNARDINO CO	HEALTH CENTER OLD HIGHSCHOOL BLDG	ALL	✓	✓	✓		
BEAUMONT RIVERSIDE CO	V D CLINIC 102 E 5TH ST	ALL	✓	✓	✓		
BERKELEY ALAMEDA CO	BERKELEY HOSPITAL 2001 DWIGHT WAY	ALL	✓	✓	✓		
BLYTHE RIVERSIDE CO	BLYTHE HOSPITAL 14 TH AND MARKET STS	ALL	✓	✓	✓		
BRAWLEY IMPERIAL CO	COONTY CLINIC F S A MIGRATORY CAMP	ALL	✓	✓	✓		
BRODERICK YOLO CO	CITY CLINIC 5TH AND E STS	ALL	✓	✓	✓		
BORBANK LOS ANGELES CO	HEALTH CENTER 528 NORTH OLIVE ST	ALL	✓	✓	✓		
BURLINGAME SAN MATEO CO	DISTRICT CLINIC 248 LORTON AVE	ALL	✓	✓	✓		
BOTTONWILLOW KERN CO	V D CLINIC	ALL	✓	✓	✓		
CALEXICO IMPERIAL CO	CITY CLINIC CITY HALL	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
CARPENTERIA SANTA BARBARA CO	HEALTH CENTER VETERANS MEM BLDG	ALL	✓	✓	✓		
CHICO BUTTE CO	HEALTH CENTER 246 SALEM ST	ALL	✓	✓	✓		
COLUSA COLUSA CO	COLUSA CO HOSPITAL	ALL	✓	✓	✓		
COMPTON LOS ANGELES CO	HEALTH CENTER 1301 WILLOWBROOK AVE	ALL	✓	✓	✓		
CORNING TEHAMA CO	4TH AVE CNTY CLINIC DR A H MEUSERS OFC	ALL	✓	✓	✓		
CRESCENT CITY DEL NORTE CO	350 H ST CO CLINIC DR F M STUMPS OFFICE	ALL	✓	✓	✓	✓	✓
DALY CITY SAN MATEO CO	PUBLIC HEALTH CLINIC 7375 MISSION ST	ALL	✓	✓	✓		
DELANO KERN CO	V D CLINIC	ALL	✓	✓	✓		
DINUBA TULARE CO	COUNTY HEALTH DEPT 153 WEST TULARE ST	ALL	✓	✓	✓		
EAST LOS ANGELES LOS ANGELES CO	HEALTH CENTER 670 SOUTH FERRIS ST	ALL	✓	✓	✓		
EL CENTRO IMPERIAL CO	CITY CLINIC COURTHOUSE	ALL	✓	✓	✓		
EL MONTE LOS ANGELES CO	HEALTH CENTER 333 CALIFORNIA ST	ALL	✓	✓	✓		
EL MONTE LOS ANGELES CO	RUTH HOME HOSPITAL 831 NO GILMAN RD	ALL	✓	✓	✓	✓	✓
EUREKA HUMBOLDT CO	HUMBOLDT CO HOSP 2200 HARRISON AVE	ALL	✓	✓	✓		
FAIRFIELD SOLANO CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
FRESNO FRESNO CO	CITY CLINIC 1039 H ST	ALL	✓	✓	✓		
FRESNO FRESNO CO	FRESNO CO HOSP 4461 VENTURA AVE	ALL	✓	✓	✓		
GILROY SANTA CLARA CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
GLENDALE LOS ANGELES CO	HEALTH CENTER 200 W LEXINGTON DR	ALL	✓	✓	✓		
GRASS VALLEY NEVADA CO	CITY COUNTY CLINIC 255 SOUTH AUBURN ST	ALL	✓	✓	✓		
GRASS VALLEY NEVADA CO	RECEIVING HOSPITAL 118 BUSH ST	ALL	✓	✓		✓	✓
GRIDLEY BUTTE CO	CITY CLINIC DR H T CAREYS OFFICE	ALL	✓	✓	✓		
GUADALUPE SANTA BARBARA CO	COUNTY CLINIC 103 E THIRD ST	ALL	✓	✓	✓	✓	✓
HALF MOON BAY SAN MATEO CO	DISTRICT CLINIC DR BOORLEYS OFFICE	ALL	✓	✓	✓		
HANFORD KINGS CO	KINGS CO HOSPITAL LACEY BLVD	ALL	✓	✓	✓		

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CALIFORNIA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
HEALOSBURG SONOMA CO	COUNTY CLINIC 415 CENTER ST	ALL	✓	✓	✓		
HUNTINGTON PARK LOS ANGELES CO	SAN ANTONIO H CENTER 7300 SANTA FE AVE	ALL	✓	✓	✓		
INOIO RIVERSIDE CO	HEALTH CENTER 402 BESO ST	ALL	✓	✓	✓		
INGLEWOOD LOS ANGELES CO	HEALTH CENTER 101 S GREVILLEA ST	ALL	✓	✓	✓		
JOLON MONTEREY CO	V D CLINIC CAMP NACIMIENTO	ALL	✓		✓		
KING CITY MONTEREY CO	CITY CLINIC 319 BROADWAY	ALL	✓	✓	✓		
LANCASTER LOS ANGELES CO	HEALTH CENTER 311 WEST 10TH ST	ALL	✓	✓	✓		
LOMA LINOA SAN BERNARDINO CO	CITY DISPENSARY 255 STEWART ST	ALL	✓	✓	✓		
LOMPOC SANTA BARBARA CO	CITY CLINIC 122 NORTH H ST	ALL	✓	✓	✓	✓	
LONG BEACH LOS ANGELES CO	CITY HEALTH DEPT 404 CITY HALL	ALL	✓	✓	✓		
LOS ANGELES LOS ANGELES CO	CEDARS LEBANON HOSP 1306 NO BERANDO AVE	ALL	✓	✓	✓	✓	✓
LOS ANGELES LOS ANGELES CO	CHILORENS HOSPITAL 4614 SUNSET BLVD	C	✓		✓	✓	
LOS ANGELES LOS ANGELES CO	CO GENERAL HOSP 1200 NORTH STATE ST	ALL	✓	✓	✓	✓	
LOS ANGELES LOS ANGELES CO	CO HLTH DEPT CLINICS HALL OF JUSTICE	ALL	✓	✓	✓		
LOS ANGELES LOS ANGELES CO	CO OSTEOPATHIC HOSP 1100 N MISSION RD	ALL	✓	✓	✓	✓	
LOS ANGELES LOS ANGELES CO	GOOD HOPE CLINIC 1241 SHATTO ST	ALL	✓	✓		✓	
LOS ANGELES LOS ANGELES CO	GRAVES MEMORIAL DISP 737 NORTH BROADWAY	ALL	✓	✓		✓	✓
LOS ANGELES LOS ANGELES CO	L A MATERNITY 225 NO MAIN ST	ALL		✓	✓	✓	✓
LOS ANGELES LOS ANGELES CO	MENS CENTRAL CLINIC 116 TEMPLE ST RM 200	M	✓	✓	✓		
LOS ANGELES LOS ANGELES CO	SOUTHEAST POLYCLINIC CENTRAL AVE AT 55 ST	N	✓	✓	✓		
LOS ANGELES LOS ANGELES CO	WEST L A CLINIC 1620 PURDUE AVE	ALL	✓	✓	✓		
LOS ANGELES LOS ANGELES CO	WHITE MEM CLINIC 312 NORTH BOYLE AVE	ALL	✓	✓		✓	
LOS ANGELES LOS ANGELES CO	WOMENS CENTRAL CLIN 116 WEST TEMPLE ST	F	✓	✓	✓		
LOS MOLINOS TEHAMA CO	COUNTY CLINIC DR J H BELYEAS OFC	ALL	✓	✓	✓		
MADERA MADERA CO	MADERA CO HOSPITAL ROUTE 2	ALL	✓	✓	✓	✓	✓

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
MARTINEZ CONTRA COSTA CO	COUNTY HOSPITAL	ALL	✓	✓	✓		
MARYSVILLE YUBA CO	SUTTER YUBA CLINIC 309 C ST	ALL	✓	✓	✓		
MERCED MERCED CO	COUNTY HOSPITAL 15TH STREET	ALL	✓	✓	✓	✓	
MODESTO STANISLAUS CO	COUNTY HOSPITAL H STREET	ALL	✓	✓	✓	✓	
MONROVIA LOS ANGELES CO	HEALTH CENTER 211 W COLORADO BLVD	ALL	✓	✓	✓		
MONTEBELLO LOS ANGELES CO	SIMONS CLINIC SIMONS BRICKYARD	ALL	✓	✓	✓		
MONTEREY MONTEREY CO	CITY CLINIC ABREGO AND WEBSTER	ALL	✓	✓	✓		
OAKLAND ALAMEDA CO	CITY CLINIC 282 EIGHTH ST	ALL	✓	✓	✓		
OAKLAND ALAMEDA CO	E BAY CHILDRENS HOSP 5105 OOVER ST	ALL	✓	✓		✓	
OAKLAND ALAMEDA CO	PAC PROTECTIVE SOC 2118 EAST 21ST ST	ALL	✓	✓		✓	
ONTARIO SAN BERNARDINO CO	HEALTH CENTER CITY HALL BLDG	ALL	✓	✓	✓		
ORANGE ORANGE CO	COUNTY CLINIC ROUTE 2 101 HIGHWAY	ALL	✓	✓	✓		
OROVILLE BUTTE CO	BUTTE CO HOSPITAL 1453 MYERS ST	ALL	✓	✓	✓		
OROVILLE BUTTE CO	DR B C EPPERSON OFC 1453 MYERS ST	ALL	✓	✓	✓		
PARADISE BUTTE CO	CITY CLINIC DR LORDS OFFICE	ALL	✓	✓	✓		
PASADENA LOS ANGELES CO	CITY HEALTH DEPT 38 CONGRESS ST	ALL	✓	✓	✓	✓	
PASO ROBLES SAN LUIS OBISPO	DR A SHERSHOW OFFICE 242 SPRING ST	ALL	✓	✓	✓		
PESCADERO SAN MATEO CO	CITY CLINIC DR C V THOMPSONS OFC	ALL	✓	✓	✓		
PETALUMA SONOMA CO	COUNTY CLINIC 17 4TH ST	ALL	✓	✓	✓		
PITTSBURG CONTRA COSTA CO	CITY CLINIC 263 EAST 8TH ST	ALL	✓	✓	✓		
POMONA LOS ANGELES CO	HEALTH CENTER 280 WEST FIFTH ST	ALL	✓	✓	✓		
PORTERVILLE TULARE CO	CITY CLINIC 531 A MAIN ST	ALL	✓	✓	✓		
QUINCEY PLUMAS CO	PLUMAS CO HOSPITAL	ALL	✓	✓	✓		
RED BLUFF TEHAMA CO	THOMPSON CLINIC 410 PINE ST	ALL	✓	✓	✓		
REDDING SHASTA CO	SHASTA CO HOSPITAL	ALL	✓	✓	✓		

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CALIFORNIA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
REDWOOD CITY SAN MATEO CO	DISTRICT CLINIC COURTHOUSE	ALL	✓	✓	✓		
RICHMOND CONTRA COSTA CO	HEALTH CENTER 237 NINTH ST	ALL	✓	✓	✓		
RIVERSIDE RIVERSIDE CO	RIVERSIDE CO H O COURT HOUSE	ALL	✓	✓	✓		
SACRAMENTO SACRAMENTO CO	MUNICIPAL CLINIC 909 FIFTH ST	ALL	✓	✓	✓		
SACRAMENTO SACRAMENTO CO	SACRAMENTO CO HOSP STOCKTON BLVD	ALL	✓	✓	✓		
SALINAS MONTEREY CO	MONTEREY CO HOSP	ALL	✓	✓	✓		
SAN BERNARDINO SAN BERNARDINO CO	COUNTY HEALTH CENTER 236 FOURTH ST	ALL	✓	✓	✓		
SAN DIEGO SAN DIEGO CO	MUNICIPAL CLINIC CIVIC CENTER	ALL	✓	✓	✓		
SAN FERNANDO LOS ANGELES CO	HEALTH CENTER 604 MACLAY AVE	ALL	✓	✓	✓		
SAN FRANCISCO SAN FRANCISCO CO	CHILDRENS HOSPITAL 3700 CALIFORNIA ST	ALL	✓	✓	✓	✓	
SAN FRANCISCO SAN FRANCISCO CO	CITY HEALTH DEPT 33 HUNT ST	ALL	✓	✓	✓		
SAN FRANCISCO SAN FRANCISCO CO	CO HOSP MAT CLINIC POTRERO AVE	A	✓	✓	✓	✓	
SAN FRANCISCO SAN FRANCISCO CO	CITY HEALTH DEPT 33 HUNT ST	ALL	✓	✓	✓		
SAN FRANCISCO SAN FRANCISCO CO	G U OIAG CENTER 101 GROVE ST	ALL	✓	✓	✓		
SAN FRANCISCO SAN FRANCISCO CO	HOMEOPATHIC CLINIC 129 HAIGHT ST	ALL	✓	✓	✓	✓	
SAN FRANCISCO SAN FRANCISCO CO	MARYS HELP HOSP 145 GUERRERO ST	ALL	✓	✓	✓	✓	
SAN FRANCISCO SAN FRANCISCO CO	MOUNT ZION CLINIC 2200 POST ST	ALL	✓	✓	✓	✓	✓
SAN FRANCISCO SAN FRANCISCO CO	ST LUKES HOSPITAL 27TH AT VALENCIA ST	A	✓	✓	✓	✓	
SAN FRANCISCO SAN FRANCISCO CO	S F POLYCLINIC 1535 JACKSON ST	ALL	✓	✓		✓	
SAN FRANCISCO SAN FRANCISCO CO	STANFORD UNIV HOSP 2398 SACRAMENTO ST	ALL	✓	✓	✓	✓	✓
SAN FRANCISCO SAN FRANCISCO CO	UNIV OF CALIF O P D 2ND AT PARNASSUS AVE	ALL	✓	✓	✓	✓	✓
SAN JACINTO RIVERSIDE CO	HEALTH CENTER	ALL	✓	✓	✓		
SAN JOSE SANTA CLARA CO	COUNTY HEALTH DEPT HALL OF JUSTICE	ALL	✓	✓	✓		
SAN JOSE SANTA CLARA CO	SANTA CLARA CO HOSP	ALL	✓	✓	✓		
SAN LEANDRO ALAMEDA CO	FAIRMONT CLINIC 22247 FOOTHILL BLVD	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
SAN LUIS OBISPO SAN LUIS OBISPO	COUNTY HEALTH DEPT 1009 MORRO ST	ALL	✓	✓	✓		
SAN MATEO SAN MATEO CO	COMMUNITY HOSPITAL 39TH AVENUE	ALL	✓	✓	✓		
SAN PEDRO LOS ANGELES CO	CITY CLINIC 599 WEST SEVENTH ST	ALL	✓	✓	✓		
SANTA ANA ORANGE CO	CITY DIAG CENTER COURT HOUSE	ALL	✓	✓	✓		
SANTA BARBARA SANTA BARBARA CO	HEALTH CENTER 507 SANTA BARBARA ST	ALL	✓	✓	✓		
SANTA CRUZ SANTA CRUZ CO	COUNTY HOSPITAL EMELINE ST	ALL	✓	✓	✓		
SANTA MARIA SANTA BARBARA CO	DISTRICT HLTH OFFICE 112 SO LINCOLN ST	ALL	✓	✓	✓		
SANTA MARIA SANTA BARBARA CO	SANTA MARIA HOSPITAL PARKVIEW ST	ALL	✓	✓	✓		
SANTA MONICA LOS ANGELES CO	HEALTH CENTER 1525 EUCLID ST	ALL	✓	✓	✓		
SANTA ROSA SONOMA CO	COUNTY HEALTH DEPT 315 TENTH ST	ALL	✓	✓	✓		
SEBASTOPOL SONOMA CO	COUNTY HEALTH DEPT SHERIDAN LANE	ALL	✓	✓	✓		
SHASTA DAM SHASTA CO	SHASTA DAM HOSPITAL	ALL	✓	✓		✓	✓
SONOMA SONOMA CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
SONORA TUOLUMNE CO	COUNTY CLINIC	ALL	✓	✓	✓		
STOCKTON SAN JOAQUIN CO	LOCAL H DIS CLINIC 130 S AMERICAN ST	ALL	✓	✓	✓		
TAFT KERN CO	V D CLINIC	ALL	✓	✓	✓		
TURRANCE LOS ANGELES CO	HEALTH CENTER 2300 CARSON ST	ALL	✓	✓	✓		
TULARE TULARE CO	CO GENERAL HOSPITAL CO HUSPITAL GROUNDS	ALL	✓	✓	✓		
UKIAH MENDOCINO CO	COUNTY CLINIC DR H D CLELLANOS DFC	ALL	✓	✓		✓	✓
VALLEJO SOLANO CO	COUNTY CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
VAN NUYS LOS ANGELES CO	V D CLINIC 14410 SYLVAN ST	ALL	✓	✓	✓		
VENICE LOS ANGELES CO	V D CLINIC 685 VENICE BLVD	ALL	✓	✓	✓		
VENTURA VENTURA CO	CITY HEALTH DEPT 121 N FIR ST	ALL	✓	✓	✓		
VENTURA VENTURA CO	COUNTY HOSP	ALL	✓	✓	✓		
VENTURA VENTURA CO	COUNTY V D CLINIC LOMA VISTA RD	ALL	✓	✓	✓	✓	

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
VISALIA TULARE CO	COUNTY HEALTH DEPT 1501 WEST MAIN ST	ALL	✓	✓	✓		
WASCO KERN CO	HEALTH CENTER	ALL	✓	✓	✓		
WATTS LOS ANGELES CO	V D CLINIC FOR MEN CITY HALL	M	✓	✓	✓		
WATTS LOS ANGELES CO	V D CLINIC FOR WOMEN 1513 E 103RD ST	FC	✓	✓	✓		
WEST HOLLYWOOD LOS ANGELES CO	HEALTH CENTER 730 N SAN VINCENTE	ALL	✓	✓	✓		
WHITTIER LOS ANGELES CO	HEALTH CENTER 402 S GREENLEAF ST	ALL	✓	✓	✓		
WILLIAMS COLUSA CO	CITY CLINIC DR C M KEITHS OFFICE	ALL	✓	✓	✓	✓	
WILLOWS GLENN CO	GLENN CO HOSPITAL	ALL	✓	✓	✓		
WILMINGTON LOS ANGELES CO	COUNTY V D CLINIC 212 F STREET	ALL	✓	✓	✓		
WOODLAND YOLO CO	YOLO CO HOSPITAL COURTHOUSE ROOM 102	ALL	✓	✓	✓		
YREKA SISKIYOU CO	COUNTY CLINIC 303 N OREGON ST	ALL	✓	✓		✓	✓
YREKA SISKIYOU CO	YREKA CO HOSPITAL	ALL	✓	✓	✓		
	COLORADO						
COLORADO SPRINGS EL PASO CO	COUNTY P H CLINIC COURTHOUSE	ALL	✓	✓	✓		
DENVER DENVER CO	DENVER HEALTH CLINIC DENVER GENERAL HOSP	ALL	✓	✓	✓		
DENVER DENVER CO	COLO GEN HOSP CLINIC 4200 EAST 9TH AVE	ALL	✓		✓		
FORT COLLINS LARIMER CO	COUNTY P H CLINIC 125 LINDEN ST	ALL	✓	✓	✓		
FORT LUPTON WELD CO	V D CLINIC	ALL	✓	✓	✓		
FOWLER OTERO CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
GREELEY WELD CO	COUNTY P H CLINIC 1528 11TH AVE	ALL	✓	✓	✓		
LA JUNTA OTERO CO	COUNTY HEALTH DEPT 17 WEST 4TH ST	ALL	✓	✓	✓		
MANZANOLA OTERO CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
PUEBLO PUEBLO CO	COUNTY P H CLINIC CITY HALL	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
ROCKY FORD OTERO CO	COUNTY P H CLINIC 9TH AND WALNUT STS	ALL	✓	✓	✓		
SAN LOUIS COSTILLA CO	COUNTY CLINIC	ALL	✓	✓	✓		
	CONNECTICUT						
ANSONIA NEW HAVEN CO	TREATMENT STATION 88 MAIN STREET	ALL	✓		✓		
BETHEL FAIRFIELD CO	TREATMENT STATION 155 GREENWOOD AVE	ALL	✓		✓		
BRANFORD NEW HAVEN CO	TREATMENT STATION 87 MAIN ST	ALL	✓		✓		
BRIDGEPORT FAIRFIELD CO	V D CLINIC WELFARE BUILDING	ALL	✓	✓		✓	
BRISTOL HARTFORD CO	V D CLINIC 110 SOUTH ST	ALL	✓	✓	✓		
BROAD BROOK HARTFORD CO	TREATMENT STATION DR ROBINSONS OFFICE	ALL	✓		✓		
CANAAN LITCHFIELD CO	TREATMENT STATION MAIN STREET	ALL	✓		✓		
CHESHIRE NEW HAVEN CO	TREATMENT STATION MAPLE AVENUE	ALL	✓		✓		
CLINTON MIDDLESEX CO	TREATMENT STATION 20 COMMERCE ST	ALL	✓		✓		
COLCHESTER NEW LONDON CO	TREATMENT STATION 16 NORWICH AVE	ALL	✓		✓		
CORNWALL BRIDGE LITCHFIELD CO	TREATMENT STATION DR J EVARTS OFFICE	ALL	✓		✓		
DANBURY FAIRFIELD CO	TREATMENT STATION 158 DEER HILL AVE	ALL	✓		✓		
DANIELSON WINDHAM CO	TREATMENT STATION 7 BROAD ST	ALL	✓		✓		
DARIEN FAIRFIELD CO	TREATMENT STATION 188 POST ROAD	ALL	✓		✓		
DEEP RIVER MIDDLESEX CO	TREATMENT STATION 111 KIRTLAND ST	ALL	✓		✓		
DERBY NEW HAVEN CO	TREATMENT STATION 13 ELIZABETH ST	ALL	✓		✓		
EAST HARTFORD HARTFORD CO	TREATMENT STATION 27 WELLS AVE	ALL	✓		✓		
ESSEX MIDDLESEX CO	TREATMENT STATION 5 SOUTH MAIN	ALL	✓		✓		
FAIRFIELD FAIRFIELD CO	TREATMENT STATION 133 REEF RD	ALL	✓		✓		
FARMINGTON HARTFORD CO	TREATMENT STATION ELM TREE INN	ALL	✓		✓		

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CONNECTICUT

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
GRANBY HARTFORD CO	TREATMENT STATION OR PENOLETONS OFFICE	ALL	✓		✓		
GREENWICH FAIRFIELD CO	CITY HOSPITAL ASSN WILLIAM ST	ALL	✓		✓		
GREENWICH FAIRFIELD CO	MUNICIPAL HOSPITAL PARSONAGE ROAD	ALL	✓	✓	✓		
GROTON NEW LONDON CO	TREATMENT STATION 242 THAMES ST	ALL	✓		✓		
HAMPTON WINDHAM CO	TREATMENT STATION OR A O MARSHS OFFICE	ALL	✓		✓		
HARTFORD HARTFORD CO	BD OF HEALTH CLINIC 39 ARCH ST	ALL	✓	✓	✓		
HARTFORD HARTFORD CO	DISPENSARY 56 WINTHROP ST	ALL	✓	✓		✓	
HARTFORD HARTFORD CO	MUNICIPAL HOSPITAL 4 HOLCOMB ST	ALL	✓		✓		
HARTFORD HARTFORD CO	ST FRANCIS HOSPITAL 114 WOODLAND STREET	ALL	✓			✓	
LITCHFIELD LITCHFIELD CO	TREATMENT STATION 80 WEST ST	ALL	✓		✓		
MANCHESTER HARTFORD CO	TREATMENT STATION 689 MAIN ST	ALL	✓		✓		
MERIDEN NEW HAVEN CO	V D CLINIC 181 COOK AVE	ALL	✓		✓		
MIDDLETOWN MIDDLESEX CO	TREATMENT STATION 28 CRESCENT ST	ALL	✓		✓		
MIDDLETOWN MIDDLESEX CO	V D CLINIC 51 BROAD ST	ALL	✓	✓	✓		
MOODUS MIDDLESEX CO	TREATMENT STATION DR HORSEFIELDS OFC	ALL	✓		✓		
NAUGATUCK NEW HAVEN CO	TREATMENT STATION 83 MEADOWS ST	ALL	✓		✓		
NEW BRITAIN HARTFORD CO	BD OF HEALTH CLINIC GENERAL HOSPITAL	ALL	✓	✓	✓		
NEW CANAAN FAIRFIELD CO	TREATMENT STATION 80 SOUTH AVE	ALL	✓		✓		
NEW HARTFORD LITCHFIELD CO	TREATMENT STATION 14 MAIN ST	ALL	✓		✓		
NEW HAVEN NEW HAVEN CO	MUNICIPAL CLINIC 106 WILLIAM ST	ALL	✓	✓		✓	
NEW HAVEN NEW HAVEN CO	GRACE HOSP PEDIATRIC 1418 CHAPEL ST	C	✓		✓		
NEW HAVEN NEW HAVEN CO	HOSP DISP MED CLINIC 789 HOWARD AVE	A	✓	✓	✓		
NEW HAVEN NEW HAVEN CO	HOSP DISP PED CLINIC 789 HOWARD AVE	C	✓	✓	✓		
NEW HAVEN NEW HAVEN CO	GRACE HOSP UROL 1418 CHAPEL ST	A		✓	✓		
NEWINGTON HARTFORD CO	TREATMENT STATION 866 MAIN ST	ALL	✓		✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
NEW LONOON NEW LONDON CO	V O CLINIC 116 HUNTINGTON ST	ALL	✓	✓	✓		
NEW MILFORO LITCHFIELO CO	TREATMENT STATION 50 BRIOGE ST	ALL	✓		✓		
NEWTOWN FAIRFIELD CO	TREATMENT STATION MAIN STREET	ALL	✓		✓		
NIANTIC NEW LONOON CO	TREATMENT STATION 61 MAIN ST	ALL	✓		✓		
NORFOLK LITCHFIELO CO	TREATMENT STATION GREENWOODS ROAO WEST	ALL	✓		✓		
NORWALK FAIRFIELO CO	V O CLINIC 79 WASHINGTON ST	ALL	✓	✓	✓		
NORWICH NEW LONDON CO	W W BACKUS HOSPITAL 326 WASHINGTON ST	ALL	✓	✓	✓		
OLD LYME NEW LONDON CO	TREATMENT STATION DR DEVITTS OFFICE	ALL	✓		✓		
PAWCATUCK NEW LONDON CO	TREATMENT STATION 101 WEST BROAD ST	ALL	✓		✓		
PORTLANO MIOOLESEX CO	TREATMENT STATION 309 MAIN ST	ALL	✓		✓		
PUTNAM WINDHAM CO	TREATMENT STATION 66 MAIN ST	ALL	✓		✓		
ROCKVILLE TOLLAND CO	TREATMENT STATION 70 PROSPECT STREET	ALL	✓		✓		
SIMSBURY HARTFORO CO	TREATMENT STATION DR MURPHYS OFFICE	ALL	✓		✓		
SOUTHINGTON HARTFORO CO	TREATMENT STATION DR SIMMONS OFFICE	ALL	✓		✓		
STAFFORD SPRINGS TOLLAND CO	TREATMENT STATION 106 EAST MAIN ST	ALL	✓		✓		
STAMFORD FAIRFIELD CO	STAMFORD HOSPITAL	ALL	✓	✓	✓		
STRATFORD FAIRFIELD CO	TREATMENT STATION 1949 MAIN ST	ALL	✓		✓		
SUFFIELD HARTFORD CO	TREATMENT STATION 339 MAIN ST	ALL	✓		✓		
THOMPSONVILLE HARTFORD CO	TREATMENT STATION 75 N MAIN ST	ALL	✓		✓		
TORRINGTON LITCHFIELD CO	TREATMENT STATION 24 CHURCH ST	ALL	✓		✓		
WALLINGFORD NEW HAVEN CO	V D CLINIC 235 CENTER ST	ALL	✓		✓		
WATERBURY NEW HAVEN CO	CHASE MEMORIAL DISP 43 FIELD ST	ALL	✓	✓	✓		
WATERBURY NEW HAVEN CO	ST MARYS HOSPITAL 56 FRANKLIN ST	ALL	✓		✓		
WATERTOWN LITCHFIELO CO	TREATMENT STATION 429 MAIN ST	ALL	✓		✓		
WEST HARTFORO HARTFORO CO	TREATMENT STATION 69 S MAIN ST	ALL	✓		✓		

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CONNECTICUT - DELAWARE

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
WESTPORT FAIRFIELD CO	TREATMENT STATION 44 CHURCH LANE	ALL	✓		✓		
WETHERSFIELD HARTFORD CO	TREATMENT STATION 330 MAIN ST	ALL	✓		✓		
WILLIMANTIC WINDHAM CO	TREATMENT STATION 672 MAIN ST	ALL	✓		✓		
WINDSOR HARTFORD CO	TREATMENT STATION 18 ELM ST	ALL	✓		✓		
WINDSOR LOCKS HARTFORD CO	TREATMENT STATION 4 OAK ST	ALL	✓		✓		
WINSTED LITCHFIELD CO	TREATMENT STATION 350 MAIN ST	ALL	✓		✓		
WOODBURY LITCHFIELD CO	TREATMENT STATION OR H S ALLENS OFFICE	ALL	✓		✓		
	DELAWARE						
DOVER KENT CO	BD OF HEALTH CLINIC 320 WEST DIVISION ST	ALL	✓	✓	✓		
FRANKFORD SUSSEX CO	BD OF HEALTH CLINIC EAGLE POULTRY CO	ALL	✓	✓	✓		
GEORGETOWN SUSSEX CO	BD OF HEALTH CLINIC THE CIRCLE	ALL	✓	✓	✓		
MIDDLETOWN NEW CASTLE CO	STATE BD OF HEALTH OLD ACADEMY BLDG	ALL	✓	✓	✓		
MILFORD SUSSEX CO	BD OF HEALTH CLINIC 111 WEST 3RD ST	ALL	✓	✓	✓		
NEWARK NEW CASTLE CO	BD OF HEALTH CLINIC EAST MAIN ST	ALL	✓	✓	✓		
REHOBOTH SUSSEX CO	STATE BD OF HEALTH OLD SCH REHOBOTH AVE	ALL	✓	✓	✓		
SEAFORD SUSSEX CO	BD OF HEALTH CLINIC NORTH AND POPLAR STS	ALL	✓	✓	✓		
SMYRNA KENT CO	BD OF HEALTH CLINIC WELFARE HOME	ALL	✓	✓	✓		
WILMINGTON NEW CASTLE CO	DELAWARE HOSPITAL 14TH AND WASH STS	ALL	✓	✓		✓	
WILMINGTON NEW CASTLE CO	MEMORIAL HOSPITAL 1501 VAN BOREN ST	ALL	✓	✓		✓	
WILMINGTON NEW CASTLE CO	ST FRANCIS HOSPITAL 8TH AND CLAYTON STS	ALL	✓	✓		✓	
WILMINGTON NEW CASTLE CO	STATE BD OF HEALTH 301 SHIPLEY ST	N	✓	✓	✓		
WILMINGTON NEW CASTLE CO	WILMINGTON GEN HOSP CHESTNUT AT BROOM ST	ALL	✓	✓		✓	

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N - NEGROES ONLY O - CHILDREN ONLY F - FEMALES ONLY AS INDICATED IN TITLE OF CLINIC

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
	DISTRICT OF COLUMBIA						
WASHINGTON	CHILDRENS HOSPITAL 13TH AND W STS N W	C	✓	✓	✓	✓	
WASHINGTON	COLUMBIA HOSP CLINIC 2425 L ST N W	F	✓	✓		✓	
WASHINGTON	EMERGENCY HOSPITAL 1711 NEW YORK AVE NW	ALL	✓	✓	✓	✓	✓
WASHINGTON	EPISCOPAL HOSPITAL 1147FIFTEENTH ST N W	ALL	✓			✓	
WASHINGTON	FREEDMANS HOSPITAL 6TH AND BRYANT ST NW	ALL	✓	✓	✓		
WASHINGTON	GALLINGER HOSPITAL 19TH AND C STS S E	A	✓		✓		
WASHINGTON	GARFIELD HOSPITAL 11TH AND FLA AVE NW	A	✓	✓	✓	✓	
WASHINGTON	GEORGETOWN UNIV HOSP 35TH AND N STS N W	ALL	✓	✓	✓		✓
WASHINGTON	G WASH UNIV HOSP 1339 H ST N W	A	✓	✓	✓	✓	
WASHINGTON	MAT CHILD HYG CENTER ADDISON SCHOOL N W	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER BARRVILLE SCHOOL N E	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CLINIC BURROUGHS SCHOOL N E	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER FREEDMANS HOSPITAL	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER 8TH AT SHEPHERD ST	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER GALLINGER HOSPITAL	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER 824 U STREET S E	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CLINIC 2237 NICHOLS AVE S E	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER WEIGHTMAN SCHOOL N W	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER 1364 FLORIDA AVE NE	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER 900 MARYLAND AVE N E	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER UELA AND I STS S W	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER 16 0 ST N W	C F	✓	✓	✓		
WASHINGTON	MAT CHILD HYG CENTER 1230 9TH ST N W	C F	✓	✓	✓		

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DISTRICT OF COLUMBIA – FLORIDA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
WASHINGTON	MAT CHILD HYG CENTER THIRD AND G STS S E	C F	✓	✓	✓		
WASHINGTON	NORTH CENTRAL CLINIC 7TH AND P STREETS NW	ALL	✓	✓	✓		
WASHINGTON	PROVIDENCE HOSPITAL 2ND AND D STS S E	ALL	✓	✓	✓	✓	✓
WASHINGTON	HEALTH CENTER DELA AND I ST S W	ALL	✓	✓	✓		
	FLORIDA						
APALACHICOLA FRANKLIN CO	COUNTY HEALTH DEPT	ALL	✓		✓		
APOPKA ORANGE CO	COUNTY HEALTH CENTER	ALL	✓		✓		
AVON PARK HIGHLANDS CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
BALDWIN DUVAL CO	COUNTY HEALTH UNIT BALDWIN COL CHURCH	ALL	✓	✓	✓		
BARTOW POLK CO	COUNTY HOSPITAL	ALL	✓		✓	✓	
BELLE GLADE PALM BEACH CO	COUNTY CLINIC	ALL	✓	✓		✓	
BELLE GLADE PALM BEACH CO	V D CONTROL CLINIC OKEECHOBEE CAMP	N	✓	✓	✓		
BELLE GLADE PALM BEACH CO	V D CONTROL CLINIC OSCEOLA LABOR CAMP	W	✓	✓	✓		
BOCA RATON PALM BEACH CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓		✓	
BRADENTON MANATEE CO	COUNTY CLINIC	ALL	✓		✓		
BRONSON LEVY CO	CITY HEALTH DEPT	ALL	✓	✓	✓		
BROWNSVILLE ESCAMBIA CO	HEALTH DEPT CLINIC	ALL	✓		✓		
BUNNELL FLAGLER CO	COUNTY HEALTH UNIT 2ND FLOOR COURTHOUSE	ALL	✓	✓	✓		
CALLAHAN NASSAU CO	COUNTY HEALTH UNIT BRADES STORE	ALL	✓	✓	✓		
CARRABELLE FRANKLIN CO	COUNTY HEALTH DEPT	ALL	✓		✓		
CEDAR KEYS LEVY CO	COUNTY HEALTH DEPT	ALL	✓		✓		
CENTURY ESCAMBIA CO	COUNTY HEALTH DEPT	ALL	✓		✓		
CHATTAHOOCHIE GADSDEN CO	CO HEALTH UNIT	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
CHIEFLAND LEVY CO	COUNTY HEALTH UNIT CHIEFLAND SCHOOL	ALL	✓		✓		
CLEARWATER PINELLAS CO	COUNTY HEALTH UNIT HEALTH CENTER	ALL	✓		✓		
CLERMONT LAKE CO	COUNTY HEALTH DEPT	ALL	✓		✓		
COTTONDALE JACKSON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CRAWFORDVILLE WAKULLA CO	CITY CLINIC	ALL	✓		✓		
CRESTVIEW OKALOOSA CO	COUNTY HEALTH DEPT	ALL	✓		✓		
DEFUNIAK SPRINGS WALTON CO	HEALTH DEPT CLINIC	ALL	✓	✓	✓		
DELRAY PALM BEACH CO	COUNTY CLINIC COLORED SCHOOLHOUSE	ALL	✓	✓		✓	
EUSTIS LAKE CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓		✓		
FERNANDINA NASSAU CO	COUNTY HEALTH UNIT	ALL	✓	✓	✓		
FT LAUDERDALE BROWARD CO	COUNTY HEALTH DEPT 501 S ANDREWS AVE	ALL	✓	✓	✓		
FT PIERCE ST LUCIE CO	CITY CLINIC HEALTH CENTER	ALL	✓			✓	
GAINESVILLE ALACHUA CO	CITY HEALTH DEPT	ALL	✓			✓	
GRACEVILLE JACKSON CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓	✓	✓		
GREEN COVE SPRING CLAY CO	HEALTH DEPT CLINIC HEALTH CENTER	ALL	✓	✓	✓		
GREENSBORO GADSDEN CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓		✓		
GREENWOOD JACKSON CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓	✓	✓		
GRETNA GADSDEN CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓		✓		
GROVELAND LAKE CO	COUNTY HEALTH DEPT	ALL	✓		✓		
GULF HAMMOCK LEVY CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓		✓		
HAVANA GADSDEN CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓		✓		
HILLIARD NASSAU CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
HOLLYWOOD BROWARD CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓		✓		
JACKSONVILLE DUVAL CO	BREWSTER HOSPITAL 7TH AND JEFFERSON ST	N	✓	✓		✓	
JACKSONVILLE BCH DUVAL CO	COUNTY HEALTH UNIT BEACH CL COL SCHOOL	ALL	✓	✓	✓		

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FLORIDA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
JACKSONVILLE OUVAL CO	OUVAL CO HOSPITAL 710 W 10TH ST	ALL	✓	✓	✓		
JASPER HAMILTON CO	COUNTY HEALTH OEPT	ALL	✓		✓		
KEY WEST MONROE CO	COUNTY HEALTH OEPT 1300 UNITED ST	ALL	✓	✓	✓		
KISSIMMEE OSCEOLA CO	COUNTY HEALTH OEPT HEALTH CENTER	ALL	✓	✓	✓		
LAKELAND POLK CO	CITY HEALTH OEPT 809 N KENTUCKY AVE	ALL	✓	✓	✓		
LAKE PLACID HIGHLANDS CO	COUNTY HEALTH OEPT	ALL	✓		✓		
LEESBURG LAKE CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓		✓		
MACCLENNY BAKER CO	COUNTY HEALTH DEPT	ALL	✓		✓		
MARIANNA JACKSON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
MIAMI DADE CO	CITY CLINIC 910 COURTHOUSE	ALL	✓	✓	✓	✓	
MIAMI DADE CO	DADE CO HOSPITAL ROUTE 2	ALL	✓	✓	✓		
MILTON SANTA ROSA CO	HEALTH DEPT CLINIC	ALL	✓	✓	✓		
MOLINO ESCAMBIA CO	COUNTY HEALTH OEPT HEALTH CENTER	ALL	✓	✓		✓	
MOORE HAVEN GLADES CO	COUNTY HEALTH OEPT	ALL	✓	✓	✓		
MOUNT DORA LAKE CO	COUNTY HEALTH OEPT	ALL	✓		✓		
ORLANDO ORANGE CO	CITY HEALTH DEPT CITY HALL	ALL	✓	✓	✓	✓	✓
OTTER CREEK LEVY CO	COUNTY HEALTH DEPT	ALL	✓		✓		
PAHOKEE PALM BEACH CO	COUNTY CLINIC	ALL	✓	✓		✓	
PAHOKEE PALM BEACH CO	EVERGLADES MIG H CEN P O BOX 818	ALL	✓	✓	✓		
PAHOKEE PALM BEACH CO	V D CONTROL CLINIC OKEECHOBEE CAMP	ALL	✓		✓		
PANAMA CITY BAY CO	COUNTY HEALTH OEPT 315 MCKENZIE AVE	ALL	✓	✓	✓		
PENSACOLA ESCAMBIA CO	COUNTY HEALTH OEPT 803 N PALAFOX ST	ALL	✓	✓	✓		
PERRY TAYLOR CO	COUNTY HEALTH OEPT	ALL	✓	✓		✓	
PLANT CITY HILLSBOROUGH CO	CO HEALTH OEPT MAYS BLDG	ALL	✓	✓	✓		
POMPANO BROWARD CO	COUNTY HEALTH DEPT CLINIC BLDG	ALL	✓		✓		

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CITY, AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
POMPANO BROWARD CO	MIGRATORY LABOR CL MIGRATORY LABOR CAMP	W	✓		✓		
PORT ST JOE GULF CO	COUNTY HEALTH DEPT KENNEYS MILL 3RD ST	ALL	✓			✓	
PORT ST JOE GULF CO	COUNTY HEALTH DEPT	ALL	✓		✓		
PUNTA GORDA CHARLOTTE CO	COUNTY CLINIC	ALL	✓		✓		
QUINCY GADSDEN CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓		✓		
RIVER JUNCTION GADSDEN CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓		✓		
SAFETY HARBOR PINELLAS CO	COUNTY HEALTH DEPT MAIN STREET	ALL	✓		✓		
ST AUGUSTINE ST JOHNS CO	FLAGLER HOSPITAL TREMERTON ST	ALL	✓			✓	
ST CLOUD OSCEOLO CO	COUNTY HEALTH UNIT	ALL	✓		✓		
ST PETERSBURG PINELLAS CO	CITY HEALTH DEPT 440 SECOND AVE N	W	✓	✓	✓		
ST PETERSBURG PINELLAS CO	CO COLORED CLINIC 1340 22ND ST S	N	✓	✓	✓		
ST PETERSBURG PINELLAS CO	CO HEALTH DEPT 824 ARLINGTON AVE	ALL	✓	✓	✓		
SANFORD SEMINOLE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SARASOTA SARASOTA CO	CITY CO WELFARE BD COMMUNITY CENTER BLD	ALL	✓	✓	✓	✓	
SEBRING HIGHLANDS CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SHADY GROVE TAYLOR CO	COUNTY HEALTH DEPT	ALL	✓		✓		
SNEADS JACKSON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SOPCHOPPY WAKULLA CO	COUNTY HEALTH DEPT	ALL	✓		✓		
STARKE BRADFORD CO	CO VD CONTROL CLINIC COUNTY COURT HOUSE	ALL	✓	✓	✓		
STEINHATCHEE TAYLOR CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓	✓	✓		
TALLAHASSEE LEON CO	COUNTY HEALTH DEPT 323 E GAINES ST	ALL	✓	✓	✓		
TAMPA HILLSBOROUGH CO	CO HEALTH DEPT 1301 FLORIDA AVENUE	ALL	✓	✓	✓		
TAMPA HILLSBOROUGH CO	V D CLINIC 1420 TAMPA ST	ALL	✓	✓	✓		
TARPON SPRINGS PINELLAS CO	COUNTY HEALTH DEPT 1ST NATL BANK BLDG	ALL	✓		✓		
TAVARES LAKE CO	COUNTY HEALTH DEPT	ALL	✓		✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TD *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
TRENTON GILCHRIST CO	COUNTY HEALTH UNIT 2ND FLOOR BANK BLDG	ALL	✓		✓		
UMATILLA LAKE CO	COUNTY HEALTH DEPT	ALL	✓		✓		
VENUS HIGHLANDS CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
VERO BEACH INDIAN RIVER CO	COUNTY CLINIC	ALL	✓	✓	✓		
WAKULLA WAKULLA CO	HEALTH CLINIC COUNTY HEALTH DEPT	ALL	✓		✓		
WEST PALM BEACH PALM BEACH CO	CITY HEALTH DEPT 5TH AND RAILROAD STS	ALL	✓		✓	✓	
WEST PALM BEACH PALM BEACH CO	CO SYPHILIS CLINIC 902 COMEAU BLDG	ALL	✓		✓	✓	
WEWAHITCHKA GULF CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓		✓		
WILLISTON LEVY CO	HEALTH CLINIC COUNTY HEALTH DEPT	ALL	✓		✓		
WIMAUMA HILLSBOROUGH CO	CO HEALTH DEPT HEALTH CENTER	ALL	✓		✓		
WINTER GARDEN ORANGE CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓	✓	✓		
WINTER PARK ORANGE CO	COUNTY HEALTH DEPT 104 E PARK AVE	ALL	✓	✓	✓		
YULEE NASSAU CO	COUNTY HEALTH DEPT OLD SCHOOLHOUSE	ALL	✓	✓			✓
	GEORGIA						
ACWORTH COBB CO	COUNTY CLINIC	ALL	✓		✓		
ALAMO WHEELER CO	CITY CLINIC	ALL	✓		✓		
ALBANY DOUGHERTY CO	V D CLINIC BROAD STREET ALLEY	N A	✓	✓	✓		
ALBANY DOUGHERTY CO	CO V D CLINIC 216 S JACKSON ST	C N	✓	✓	✓		
ALBANY DOUGHERTY CO	COUNTY CLINIC COURTHOUSE	W A	✓		✓		
ALMA BACON CO	CITY CLINIC	ALL	✓		✓		
ALPHARETTA FULTON CO	HEALTH CENTER	ALL	✓	✓	✓		
ALTO HABERSHAM CO	STATE CLINIC TBC SANATORIUM	ALL	✓	✓	✓		
AMERICUS SUMTER CO	COUNTY HEALTH DEPT	ALL	✓		✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
AMSTERDAM DECATUR CO	CITY CLINIC	ALL	✓		✓		
ARLINGTON CALHOUN CO	CITY CLINIC	ALL	✓		✓		
ATHENS CLARKE CO	COUNTY CLINIC CITY HALL	ALL	✓		✓		
ATLANTA FULTON CO	DR OWELLES CLINIC	N	✓		✓		
ATLANTA FULTON CO	ROCKDALE PK HLTH CEN JOHNSON ROAD	N	✓		✓		
ATLANTA FULTON CO	SOCIAL DISEASE HOSP	ALL	✓	✓	✓		
AUGUSTA RICHMOND CO	COUNTY HEALTH DEPT 501 GREENE ST	ALL	✓	✓	✓		
BAINBRIDGE DECATUR CO	CITY CLINIC	ALL	✓		✓		
BARNESVILLE LAMAR CO	COUNTY CLINIC	ALL	✓		✓		
BARWICK BROOKS CO	COUNTY CLINIC	ALL	✓		✓		
BAXLEY APPLING CO	COUNTY CLINIC HEALTH CENTER	ALL	✓		✓		
BEN HILL FULTON CO	CITY HEALTH CLINIC	ALL	✓		✓		
BLACKSHEAR PIERCE CO	CITY CLINIC	ALL	✓	✓	✓		
BLUE RIDGE FANNIN CO	V D CLINIC	ALL	✓		✓		
BRONWOOD TERRELL CO	CITY CLINIC CO HEALTH DEPT	ALL	✓		✓		
BROOKFIELD TIFT CO	CITY CLINIC	ALL	✓	✓	✓		
BROOKLET BULLOCH CO	CITY CLINIC	ALL	✓		✓		
BRUNSWICK GLYNN CO	CITY CLINIC	ALL	✓	✓	✓		
BRUNSWICK GLYNN CO	NEEDWOOD MOBILE UNIT GENERAL STORE	ALL	✓	✓	✓		
BUFORD GWINNETT CO	COUNTY CLINIC	ALL	✓	✓	✓		
BUTLER TAYLOR CO	V D CLINIC	ALL	✓		✓		
BYRON PEACH CO	COUNTY CLINIC	ALL	✓		✓		
CAIRO GRADY CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CALVARY GRADY CO	CITY CLINIC	ALL	✓		✓		
CAMILLA MITCHELL CO	CITY CLINIC	ALL	✓			✓	

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GEORGIA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY	PAY
CARNESVILLE FRANKLIN CO	CITY CLINIC	ALL	✓	✓	✓		
CARTERSVILLE BARTOW CO	COUNTY CLINIC	ALL	✓	✓	✓		
CHAMBLEE DEKALB CO	CO BOARD OF HEALTH OR MARTINS OFFICE	ALL	✓	✓	✓		
CHATTAHOOCHEE FULTON CO	CITY CLINIC COLLINS DIST H CEN	ALL	✓		✓		
CHICKAMAUGA WALKER CO	V D CLINIC CO HEALTH DEPT	ALL	✓		✓		
CHIPLEY HARRIS CO	CITY CLINIC	ALL	✓		✓		
CHULA TIFT CO	CITY CLINIC	ALL	✓	✓	✓		
CLAXTON EVANS CO	CITY HEALTH CLINIC	ALL	✓		✓		
CLAYTON RABUN CO	COUNTY CLINIC	ALL	✓	✓	✓		
COCHRAN BLECKLEY CO	CITY CLINIC	ALL	✓		✓		
COLUMBUS MUSCOGEE CO	CITY HOSPITAL	ALL	✓	✓	✓		
COLUMBUS MUSCOGEE CO	COUNTY JAIL	ALL	✓	✓	✓		
COLLEGE PARK FULTON CO	COUNTY CLINIC	ALL	✓		✓		
COROELE CRISP CO	CITY CLINIC	ALL	✓		✓		
COROELE CRISP CO	GILLESPIE HOSP OPD	ALL	✓		✓		
CORNELIA HABERSHAM CO	CITY CLINIC	ALL	✓	✓	✓		
CRESCENT MCINTOSH CO	CEDAR POINT MOBILE OYSTER FACTORY	ALL	✓	✓	✓		
CRESCENT MCINTOSH CO	CRESCENT MOBILE UNIT POST OFFICE	ALL	✓	✓	✓		
CUTHBERT RANDOLPH CO	CITY CLINIC	ALL	✓	✓		✓	
DAHLONEGA LUMPKIN CO	CITY HEALTH CLINIC	ALL	✓		✓		
DALTON WHITFIELD CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
DARIEN MCINTOSH CO	CITY CLINIC	ALL	✓	✓	✓		
DARIEN MCINTOSH CO	DARIEN MOBILE UNIT HEALTH DEPARTMENT	ALL	✓	✓	✓		
DAWSON TERRELL CO	CITY CLINIC CO HEALTH DEPT	ALL	✓		✓		
DECATUR DEKALB CO	COUNTY CLINIC 318 EAST HOWARD ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
DOERUN COLQUITT CO	CITY CLINIC	ALL	✓		✓		
DONALSONVILLE SEMINOLE CO	CITY CLINIC	ALL	✓	✓	✓		
DOUGLAS COFFEE CO	HEALTH DEPT CLINIC	ALL	✓	✓	✓		
DOUGLASVILLE DOUGLAS CO	COUNTY CLINIC	ALL	✓		✓		
EASTMAN DOOGE CO	CITY CLINIC	ALL	✓	✓	✓		
EAST POINT FULTON CO	HEALTH CENTER	ALL	✓		✓		
EATONTON PUTNAM CO	CITY CLINIC	ALL	✓		✓		
EDISON CALHOUN CO	CITY CLINIC	ALL	✓		✓		
EULONIA MCINTOSH CO	EULONIA MOBILE UNIT POST OFFICE	ALL	✓	✓	✓		
EVERETT CITY GLYNN CO	EVERETT CITY MOBILE GENERAL STORE	ALL	✓	✓	✓		
FAIRBURN FULTON CO	HEALTH CENTER	ALL	✓		✓		
FOLKSTON CHARLTON CO	COUNTY CLINIC JOHNSONS MILL	ALL	✓		✓		
FOLKSTON CHARLTON CO	SILCO MOBILE UNIT SCHOOLHOUSE	ALL	✓	✓	✓		
FT VALLEY PEACH CO	COUNTY CLINIC	ALL	✓		✓		
GAINESVILLE HALL CO	CITY CLINIC	ALL	✓	✓	✓		
GIBSON GLASCOCK CO	COUNTY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
GOUGH BURKE CO	CITY CLINIC	ALL	✓		✓		
GRANTVILLE COWETA CO	V D CLINICS	ALL	✓		✓		
GRAY JONES CO	COUNTY CLINIC	ALL	✓		✓		
GRAYMONT EMANUEL CO	COUNTY CLINIC HEALTH CENTER	ALL	✓		✓		
GREENSBORO GREENE CO	COUNTY CLINIC HEALTH DEPT	ALL	✓		✓		
GREENVILLE MERIWETHER CO	CITY CLINIC	ALL	✓		✓		
GRIFFIN SPALDING CO	SYPHILIS CLINIC COURTHOUSE	ALL	✓		✓	✓	
HAPEVILLE FULTON CO	COUNTY CLINIC	ALL	✓		✓		
HINESVILLE LIBERTY CO	CITY CLINIC	ALL	✓		✓		

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GEORGIA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
HOMERVILLE CLINCH CO	COUNTY HEALTH DEPT	ALL	✓		✓		
IRWINTON WILKINSON CO	CITY CLINIC	ALL	✓		✓		
JACKSON BUTTS	CITY CLINIC	ALL	✓		✓		
JEFFERSON JACKSON CO	CITY CLINIC	ALL	✓		✓		
JEFFERSONVILLE TWIGGS CO	HEALTH CLINIC	ALL	✓		✓		
JESUP WAYNE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
KINGSLAND CAMDEN CO	GROSS STILL MOBILE TURPENTINE STILL	ALL	✓	✓	✓		
KINGSLAND CAMDEN CO	KINGSLAND MOBILE SCHOOLHOUSE	ALL	✓	✓	✓		
KNOXVILLE CRAWFORD CO	COUNTY CLINIC	ALL	✓		✓		
LAFAYETTE WALKER CO	V D CLINIC CO HEALTH DEPT	ALL	✓		✓		
LAGRANGE TROUP CO	CITY CLINIC	ALL	✓	✓	✓		
LAKELAND LANIER CO	CITY CLINIC	ALL	✓	✓	✓		
LAVONIA FRANKLIN CO	CITY CLINIC	ALL	✓	✓	✓		
LAWRENCEVILLE GWINNETT CO	COUNTY CLINIC	ALL	✓		✓		
LEARY CALHOUN CO	CITY CLINIC	ALL	✓		✓		
LEESBURG LEE CO	V D CLINIC	ALL	✓		✓		
LESLIE SUMTER CO	COUNTY CLINIC DR WOODS OFFICE	ALL	✓		✓		
LINDALE FLOYD CO	CITY CLINIC	ALL	✓		✓		
LITHONIA DEKALB CO	CO BOARD OF HEALTH CITY HALL	ALL	✓	✓	✓		
LOUISVILLE JEFFERSON CO	CITY CLINIC	ALL	✓	✓	✓		
LUDOWICI LONG CO	CITY CLINIC	ALL	✓		✓		
LUMBER CITY TELFAIR CO	COUNTY CLINIC DOCTORS OFFICE	ALL	✓		✓		
LYONS TOOMBS CO	CITY CLINIC CO HEALTH CENTER	ALL	✓	✓	✓		
MCDONOUGH HENRY CO	COUNTY CLINIC	ALL	✓		✓		
MCRAE TELFAIR CO	COUNTY HEALTH DEPT	ALL	✓	✓		✓	

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
MACON BIBB CO	MACON HOSPITAL PINE ST	ALL	✓	✓	✓	✓	
MANCHESTER MERIWETHER CO	CITY CLINIC	ALL	✓		✓		
MARSHALLVILLE MACON CO	CITY CLINIC	ALL	✓		✓		
MERIDIAN MCINTOSH CO	MERIDIAN MOBILE UNIT POST OFFICE	ALL	✓	✓	✓		
METTER CANDLER CO	CITY CLINIC	ALL	✓		✓		
MIDVILLE BURKE CO	CITY CLINIC	ALL	✓	✓	✓		
MILLEDGEVILLE BALDWIN CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
MILLEN JENKINS CO	V D CLINIC CO HEALTH DEPT	ALL	✓			✓	
MILLHAVEN SCREVEN CO	COUNTY CLINIC OR RUSHINGS OFFICE	ALL	✓		✓		
MONROE WALTON CO	COUNTY HEALTH DEPT	ALL	✓		✓		
MONTICELLO JASPER CO	CITY CLINIC HEALTH DEPT	ALL	✓	✓	✓		
MORGAN CALHOUN CO	CITY CLINIC	ALL	✓	✓	✓		
MOULTRIE COLQUITT CO	CITY CLINIC 15 FIRST AVE N W	ALL	✓	✓	✓		
NAHUNTA BRANTLY CO	HEALTH CENTER	ALL	✓		✓		
NEWNAN COWETA CO	V D CLINIC COUNTY WELFARE BLDG	ALL	✓		✓		
NORCROSS GWINNETT CO	COUNTY CLINIC	ALL	✓		✓		
OCHLOCHNEE THOMAS CO	CITY PRENATAL CLINIC	W N	✓	✓	✓		
OMEGA TIFT CO	CITY CLINIC	ALL	✓		✓		
PALMETTO FULTON CO	HEALTH CENTER	ALL	✓		✓		
PARROTT TERRELL CO	CITY CLINIC CO HEALTH DEPT	ALL	✓		✓		
PATTERSON PIERCE CO	COUNTY CLINIC CITY HALL	ALL	✓		✓		
PEARSON ATKINSON CO	V D CLINIC	ALL	✓	✓	✓		
PELHAM MITCHELL CO	W M S CLINIC	ALL	✓			✓	
PEMBROKE BRYAN CO	COUNTY CLINIC HEALTH CENTER	ALL	✓		✓		
PLAINS SUMTER CO	COUNTY CLINIC	ALL	✓		✓		

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GEORGIA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
POWDER SPRINGS COBB CO	COUNTY CLINIC	ALL	✓		✓		
QUITMAN BROOKS CO	CITY CLINIC	ALL	✓		✓		
REYNOLDS TAYLOR CO	V D CLINIC	ALL	✓		✓		
REYNOLDSVILLE SEMINOLE CO	CITY CLINIC	ALL	✓	✓	✓		
RICEBORO LIBERTY CO	CITY CLINIC	ALL	✓		✓		
RINGGOLD CATOOSA CO	V D CLINIC HEALTH DEPT	ALL	✓		✓		
ROME FLOYD CO	CITY CLINIC	ALL	✓		✓		
ROSSVILLE WALKER CO	V D CLINIC CO HEALTH DEPT	ALL	✓		✓		
ROSWELL FULTON CO	HEALTH CENTER	ALL	✓		✓		
ROYSTON FRANKLIN CO	CITY CLINIC	ALL	✓	✓	✓		
ST GEORGE CHARLTON CO	CITY CLINIC	N	✓		✓		
SANDERSVILLE WASHINGTON CO	PRENATAL CLINIC	F	✓		✓		
SANDY SPRINGS FULTON CO	COUNTY CLINIC	ALL	✓		✓		
SARDIS BURKE CO	CITY CLINIC	ALL	✓		✓		
SASSER TERRELL CO	CITY CLINIC CO HEALTH DEPT	ALL	✓		✓		
SAVANNAH CHATHAM CO	CITY CLINIC	ALL	✓	✓	✓		
SMITHVILLE LEE CO	V D CLINIC CO HEALTH DEPT	ALL	✓		✓		
SOPERTON TREUTLEN CO	CITY HEALTH CLINIC	ALL	✓		✓		
SPARTA HANCOCK CO	DEMONSTRATION CLINIC	ALL	✓	✓	✓		
SPRINGFIELD EFFINGHAM CO	CITY CLINIC	ALL	✓		✓		
STATESBORO BULLOCH CO	CITY CLINIC	ALL	✓		✓		
STERLING GLYNN CO	STERLING MOBILE UNIT SCHOOLHOUSE	ALL	✓	✓	✓		
STOCKTON LANIER CO	CITY CLINIC	ALL	✓	✓	✓		
STONE MOUNTAIN DEKALB CO	CO BOARD OF HEALTH DR MCCURDYS OFFICE	ALL	✓	✓	✓		
SYLVANIA SCREVEN CO	V D CLINIC	ALL	✓		✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
SYLVESTER WORTH CO	CITY CLINIC	ALL	✓	✓	✓		
THOMASTON UPSON CO	COUNTY CLINIC COURTHOUSE	ALL	✓		✓		
THOMASVILLE THOMAS CO	HEALTH DEPT CLINIC	ALL	✓	✓	✓		
TIFTON TIFT CO	CITY CLINIC	ALL	✓		✓		
TOCCOA STEPHENS CO	COUNTY CLINIC	ALL	✓	✓	✓		
TOWNSEND MCINTOSH CO	AROOCK MOBILE UNIT GENERAL STORE	ALL	✓	✓	✓		
TOWNSENO MCINTOSH CO	CANNON BLUFF MOBILE SCHOOLHOUSE	ALL	✓	✓	✓		
TOWNSENO MCINTOSH CO	HARRIS NECK MOBILE GENERAL STORE	ALL	✓	✓	✓		
TOWNSENO MCINTOSH CO	JONES MOBILE UNIT SCHOOLHOUSE	ALL	✓	✓	✓		
TOWNSENO MCINTOSH CO	SHELLMANBLUFF MOBILE SCHOOLHOUSE	ALL	✓	✓	✓		
TOWNSENO MCINTOSH CO	TOWNSENO MOBILE RAILWAY STATION	ALL	✓	✓	✓		
TOWNSENO MCINTOSH CO	WARSAW MOBILE GENERAL STORE	ALL	✓	✓	✓		
TY TY TIFT CO	CITY CLINIC	ALL	✓		✓		
UNION POINT GREEN CO	CITY CLINIC	ALL	✓		✓		
VALOOSTA LOWNOES CO	CO BOARD OF HEALTH	ALL	✓	✓	✓		
VIDALIA TOOMBS CO	CITY CLINIC	ALL	✓	✓	✓		
VIDETTE BURKE CO	CITY CLINIC	ALL	✓		✓		
WARM SPRINGS MERIWETHER CO	FOUNDATION CLINIC	ALL	✓		✓		
WARSAW FULTON CO	COUNTY CLINIC	ALL	✓		✓		
WAVERLY CAMDEN CO	SPRING BLUFF MOBILE TURPENTINE STILL	ALL	✓	✓	✓		
WAVERLY CAMDEN CO	WAVERLY MOBILE UNIT POST OFFICE	ALL	✓	✓	✓		
WAVERLY HALL HARRIS CO	CITY CLINIC	ALL	✓		✓		
WAYCROSS WARE CO	COUNTY V D CLINIC	ALL	✓			✓	
WAYNESBORO BURKE CO	CITY CLINIC COURTHOUSE	ALL	✓		✓		
WAYS STATION BRYAN CO	V D CLINIC	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
WEST POINT TROUP CO	CITY CLINIC	ALL	✓		✓		
WHIGHAM GRADY CO	CITY HALL CLINIC	ALL	✓	✓	✓		
WHITE OAK CAMDEN CO	TARBORO MOBILE UNIT GENERAL STORE	ALL	✓	✓	✓		
WILLACOOCHEE ATKINSON CO	V D CLINIC	ALL	✓	✓	✓		
WINDER BARROW CO	COUNTY CLINIC	ALL	✓	✓	✓		
WOODBINE CAMDEN CO	COLESBURG MOBILE FILLING STATION	ALL	✓	✓	✓		
WOODBINE CAMDEN CO	WOODBINE MOBILE UNIT COURTHOUSE	ALL	✓	✓	✓		
WOODBINE CAMDEN CO	CITY CLINIC	ALL	✓	✓	✓		
WRENS JEFFERSON CO	CITY CLINIC	ALL	✓	✓	✓		
ZEBULON PIKE CO	CITY CLINIC	ALL	✓		✓		
	IDAHO						
BOISE ADA CO	CITY CO HEALTH UNIT 415 CAPITOL SEC BLDG	ALL	✓	✓	✓	✓	
COEUR D ALENE KOOTENAI CO	COUNTY HEALTH UNIT	ALL	✓	✓	✓		
IDAHO FALLS BONNEVILLE CO	COUNTY PHYSICIAN ROGERS BLDG	ALL	✓	✓	✓		
LEWISTON NEZ PERCE CO	N C DIST HEALTH UNIT	ALL	✓	✓	✓		
POCATELLO BANNOCK CO	COUNTY HEALTH UNIT 343 E BONNEVILLE ST	ALL	✓	✓	✓		
TWIN FALLS TWIN FALLS CO	S C DIST HEALTH UNIT 212 SECOND ST EAST	ALL	✓	✓	✓		
WALLACE SHOSHONE CO	COUNTY PHYSICIAN	ALL	✓	✓	✓		
	ILLINOIS						
ALTON MADISON CO	V D CLINIC 31A EAST BROADWAY	ALL	✓	✓	✓		
ANNA UNION CO	COUNTY V D CLINIC	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
AURORA KANE CO	V D CLINIC 52 DOWNER PLACE	ALL	✓	✓	✓		
BELLVILLE ST CLA-IR CO	COUNTY V D CLINIC COMMERCIAL BLDG	ALL	✓	✓	✓		
BERWYN COOK CO	SOCIAL HYG CLINIC 6600 W 26TH ST	ALL	✓	✓	✓		
BLOOMINGTON MCLEAN CO	V D TREATMENT CENTER AM STATE BANK BLDG	ALL	✓	✓	✓		
CAIRO ALEXANDER CO	SOCIAL HYG CLINIC MARINE HOSPITAL	ALL	✓	✓	✓		
CALUMET CITY COOK CO	TREATMENT CENTER 138 POLASKI RD	ALL	✓	✓	✓		
CHAMPAIGN CHAMPAIGN CO	PUBLIC HEALTH DISTR 307 S WRIGHT ST	ALL	✓	✓	✓		
CHICAGO COOK CO	BILLINGS HOSP CLINIC UNIV OF CHICAGO	W	✓	✓			✓
CHICAGO COOK CO	CENTRAL FREE DISP 1748 W HARRISON ST	ALL	✓	✓	✓	✓	
CHICAGO COOK CO	MED SCHOOL CLINIC 710 S WOLCOTT AVE	ALL	✓	✓	✓	✓	
CHICAGO COOK CO	CHICAGO STATE HOSP 6400 IRVING PARK	ALL	✓	✓	✓		
CHICAGO COOK CO	CHILDRENS MEM HOSP 707 FULLERTON AVE	C	✓		✓		
CHICAGO COOK CO	CO CHILDRENS HOSP 1850 W HARRISON ST	C	✓	✓	✓		
CHICAGO COOK CO	CO HOSP DERMATOLOGY 1800 W HARRISON ST	A	✓		✓		
CHICAGO COOK CO	CO HOSP NEUROLOGY 1850 W HARRISON ST	A	✓		✓		
CHICAGO COOK CO	CO HOSP OBSTETRICS 1850 W HARRISON ST	FA	✓		✓		
CHICAGO COOK CO	CO JAIL CLINIC 2600 S CALIFORNIA AV	ALL	✓	✓	✓		
CHICAGO COOK CO	EHRLICK CLINIC 1362 S HALSTED ST	ALL	✓	✓	✓		
CHICAGO COOK CO	JUVENILE HOME ASSN 5141 S MICHIGAN AVE	WC	✓	✓		✓	
CHICAGO COOK CO	GRANT HOSPITAL 551 GRANT PLACE	W	✓		✓	✓	✓
CHICAGO COOK CO	CORRECTION HOUSE CL 26TH AND CALIF AVE	ALL	✓	✓	✓		
CHICAGO COOK CO	ILL EYE EAR INFIRM 904 W ADAMS ST	ALL	✓		✓		
CHICAGO COOK CO	ILL RES AND ED HOSP 1819 WEST POLK ST	ALL	✓	✓	✓		
CHICAGO COOK CO	ILL SOC HYG LEAGUE 9 EAST HURON ST	ALL	✓	✓	✓	✓	✓
CHICAGO COOK CO	MANDEL CLINIC MICHAEL REESE HOSP	ALL	✓	✓	✓	✓	

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ILLINOIS

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY	PAY
CHICAGO COOK CO	MERCY FREE DISP 2526 CALUMET AVE	ALL	✓	✓	✓	✓	✓
CHICAGO COOK CO	MONTGOMERY WARD CLIN 747 FAIRBANKS COURT	ALL	✓	✓	✓	✓	✓
CHICAGO COOK CO	MT SINAI DISPENSARY 1519 S CALIFORNIA AV	W	✓	✓	✓	✓	✓
CHICAGO COOK CO	MUN CHILDRENS CLINIC 27 EAST 26TH ST	C	✓		✓		
CHICAGO COOK CO	MUN CHILDRENS CLINIC 4253 S STATE ST	C	✓		✓		
CHICAGO COUK CO	MUN CHILDRENS CLINIC 27 E 26TH ST	C		✓	✓		
CHICAGO COOK CO	PREMARITAL EXAM CLIN 54 W HUBBARD ST	ALL	✓	✓	✓		
CHICAGO COOK CO	PRENATAL CLINIC 27 E 26TH STREET	F	✓	✓	✓		
CHICAGO COOK CO	PRENATAL SOC HYG CL 4253 S STATE ST	F	✓	✓	✓		
CHICAGO COOK CO	SOCIAL HYG CLINIC 27 E 26TH ST	ALL	✓	✓	✓		
CHICAGO COOK CO	CITY T B SANTARIUM 5601 N CRAWFORD AVE	ALL	✓	✓	✓		
CHICAGO COOK CO	V D DIAG CLINIC 1121 S STATE ST	ALL	✓	✓	✓		
CHICAGO COOK CO	POST GRADUATE HOSP 2400 S DEARBORN ST	ALL	✓	✓		✓	
CHICAGO COOK CO	PROVIDENT HOSPITAL 426 EAST 51ST ST	ALL	✓	✓		✓	
CHICAGO COOK CO	PUBLIC HEALTH INST 159 N DEARBORN ST	ALL	✓	✓		✓	
CHICAGO COOK CO	PUBLIC HEALTH INST 129 E 31ST ST	ALL	✓	✓		✓	
CHICAGO COOK CO	ST LUKES HOSP CLINIC 1439 S MICHIGAN AVE	ALL	✓	✓		✓	
CHICAGO COOK CO	SAL ARMY MATERN HOSP 5040 N PULASKI RD	F	✓		✓		
CHICAGO COOK CO	STOCKYARDS CLINIC 734 W 47TH STREET	A	✓		✓		
CHICAGO COOK CO	V O CLINIC 5120 S PARKWAY	ALL	✓	✓	✓		
CHICAGO COOK CO	WOMEN CHILDRENS HOSP 1600 MAYPOLE AVE	ALL	✓	✓	✓	✓	✓
CHICAGO HEIGHTS COOK CO	CITY CLINIC ST JAMES HOSPITAL	ALL	✓	✓	✓		
DECATUR MACON CO	CO HOSPITAL CLINIC 2300 N EDWARDS ST	ALL	✓	✓	✓		
EAST ST LOUIS ST CLAIR CO	SOCIAL HYG CLINIC 325 E BROADWAY	ALL	✓	✓	✓		
EVANSTON COOK CO	V O CLINIC 1806 MAPLE AVE	ALL	✓	✓	✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
GALESBURG KNOX CO	CO TREATMENT CENTER GALESBURG BANK BLDG	ALL	✓	✓	✓		
GRANITE CITY MADISON CO	CO SOCIAL HYG CLINIC ST ELIZABETHS HOSP	ALL	✓	✓	✓		
HARVEY COOK CO	CITY CLINIC CITY HALL	ALL	✓	✓	✓		
HERRIN WILLIAMSON CO	TREATMENT CENTER 110 WEST CHERRY ST	ALL	✓	✓	✓		
JACKSONVILLE MORGAN CO	CO CLINIC PASSAVANT HOSPITAL	ALL	✓	✓	✓		
JOLIET WILL CO	COUNTY V D CLINIC 156 NO CHICAGO ST	ALL	✓	✓			
LA SALLE LA SALLE CO	HYGIENE INSTITUTE 151 5TH ST	ALL	✓	✓	✓		
MACOMB MCDONOUGH CO	COUNTY V D CLINIC 121 SO SIDE SQUARE	ALL	✓	✓	✓		
MATTOON COLES CO	CO TREATMENT CENTER 1630 BROADWAY	ALL	✓	✓	✓		
MAYWOOD COOK CO	SOCIAL HYG CLINIC 103 S 5TH AVE	ALL	✓	✓	✓		
METROPOLIS MASSAC CO	DR FISHERS CLINIC 313 FERRY ST	ALL	✓	✓	✓		
MOLINE ROCK ISLAND CO	SOCIAL HYG CLINIC 1530 SECOND AVE	ALL	✓	✓	✓		
NEW SHAWNEETOWN GALLATIN CO	CITY CLINIC	ALL	✓	✓	✓		
PEORIA PEORIA CO	V D CLINIC 508 MAIN ST	ALL	✓	✓	✓		
PEORIA PEORIA CO	V D CLINIC 203 CITY HALL	ALL	✓	✓	✓		
QUINCY ADAMS CO	V D CLINIC 206 MAJESTIC BLDG	ALL	✓	✓	✓		
ROBBINS COOK CO	V D TREATMENT CENTER 3421 WEST 137TH ST	ALL	✓	✓	✓		
ROCKFORD WINNEBAGO CO	HEALTH CENTER 402 MEAD BLDG	ALL	✓	✓	✓		
SPARTA RANDOLPH CO	TREATMENT CENTER 209 W JACKSON ST	ALL	✓	✓	✓		
WAUKEGAN LAKE CO	CO TREATMENT CENTER 67 WASHINGTON ST	ALL	✓	✓	✓		
	INDIANA						
ANDERSON MADISON CO	P H VENEREAL CLINIC CITY HALL	ALL	✓	✓	✓		
BICKNELL KNOX CO	P H VENEREAL CLINIC CITY HALL	ALL	✓	✓	✓		

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INDIANA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
BLOOMINGTON MONROE CO	PUBLIC HEALTH CLINIC CITY HALL	ALL	✓	✓	✓		
BOONVILLE WARRICK CO	P H VENEREAL CLINIC COURTHOUSE	ALL	✓	✓	✓		
BRAZIL CLAY CO	P H VENEREAL CLINIC CLAY CO HOSPITAL	ALL	✓		✓	✓	✓
CANNELTON PERRY CO	COUNTY V O CLINIC 7TH AND WASH STREETS	ALL	✓	✓	✓		
COLUMBUS BARTHOLOMEW CO	P H VENEREAL CLINIC COURTHOUSE	ALL	✓	✓	✓		
EAST CHICAGO LAKE CO	P H VENEREAL CLINIC CITY HALL	ALL	✓	✓	✓		
EVANSVILLE VANDERBURGH CO	P H VENEREAL CLINIC COURTHOUSE ANNEX	ALL	✓	✓	✓		
FORT WAYNE ALLEN CO	P H VENEREAL CLINIC CITY HALL 3RD FLOOR	ALL	✓	✓	✓	✓	
GARY LAKE CO	HEALTH CENTER CITY HALL	ALL	✓	✓	✓		
HAMMOND LAKE CO	P H VENEREAL CLINIC CITY HALL	ALL	✓	✓	✓		
INDIANAPOLIS MARION CO	COLEMAN HOSP CLINIC 1040 W MICH ST	F	✓	✓	✓		
INDIANAPOLIS MARION CO	VULVOVAGINITIS CLIN CITY HOSPITAL	F	✓	✓	✓		
INDIANAPOLIS MARION CO	DERM AND SYPH CLINIC CITY HOSPITAL	ALL	✓	✓	✓		
INDIANAPOLIS MARION CO	MASSIVE DOSE CLINIC CITY HOSPITAL	F	✓		✓		
INDIANAPOLIS MARION CO	P H VENEREAL CLINIC 960 LOCKE ST	C	✓	✓		✓	
INDIANAPOLIS MARION CO	RILEY CLINIC 1040 W MICH ST	C	✓	✓	✓		
INDIANAPOLIS MARION CO	ROBERT W LONG HOSP 1040 W MICH ST	WA	✓	✓	✓		
KOKOMO HOWARD CO	P H VENEREAL CLINIC 107 S UNION ST	ALL	✓	✓	✓		
MADISON JEFFERSON CO	P H VENEREAL CLINIC NO 2 ENGINE HOUSE	ALL	✓	✓	✓		
MARION GRANT CO	SOCIAL HYG CLINIC CITY HALL	ALL	✓		✓		
MUNCIE DELAWARE CO	P H VENEREAL CLINIC ANTHONY BLOCK BLDG	ALL	✓	✓	✓		
NEW ALBANY FLOYD CO	P H VENEREAL CLINIC 217 E SPRING ST	ALL	✓		✓		
PETERSBURG PIKE CO	DR JOHN T KIME 108 NO EIGHTH ST	ALL	✓	✓	✓		
PRINCETON GIBSON CO	P H VENEREAL CLINIC 115 N PRINCE ST	ALL	✓	✓	✓		
RICHMOND WAYNE CO	P H VENEREAL CLINIC 26 S 7TH ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TD *	CLINIC TREATS SYPH-ILIS	CLINIC TREATS GONOR-RHEA.	FEE SYSTEM FREE	FEE SYSTEM PART-PAY.	FEE SYSTEM PAY
SHELBYVILLE SHELBY CO	P H VENEREAL CLINIC 20 N PIKE ST	ALL	✓		✓		
SOUTH BEND ST JOSEPH CO	P H VENEREAL CLINIC 114 S LAFAYETTE BLVD	ALL	✓	✓	✓		
TERRE HAUTE VIGO CO	P H VENEREAL CLINIC CITY HALL	ALL	✓	✓		✓	
WABASH WABASH CO	P H VENEREAL CLINIC CO HOSPITAL	ALL	✓		✓		
	IOWA **						
BURLINGTON DES MOINES CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
CEDAR RAPIDS LINN CO	COUNTY CLINIC ROOM 11 COURTHOUSE	ALL	✓	✓		✓	
CLINTON CLINTON CO	COUNTY CLINIC 601 WILSON BLDG	ALL	✓	✓	✓		
DAVENPORT SCOTT CO	CO HEALTH CENTER 523 MAIN ST	ALL	✓	✓	✓		
DES MOINES POLK CO	BROADLAWNS GEN HOSP 406 CENTER ST	ALL	✓	✓	✓		
DUBUQUE DUBUQUE CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
FORT DODGE WEBSTER CO	COUNTY CLINIC 1ST AVE S AND 8TH ST	ALL	✓	✓	✓		
KEOKUK LEE CO	COUNTY CLINIC 601 MAIN ST	ALL	✓	✓	✓		
MUSCATINE MUSCATINE CO	COUNTY CLINIC 111 CEDAR ST	ALL	✓	✓	✓		
OSKALOOSA MAHASKA CO	COUNTY CLINIC 107 HIGH AVE EAST	ALL	✓	✓	✓		
OTTUMWA WAPELLO CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
SIOUX CITY WOODBURY CO	CO MEDICAL CLINIC 315 SIXTH ST	ALL	✓	✓	✓		
WASHINGTON WASHINGTON CO	COUNTY HEALTH UNIT	ALL	✓		✓		
WATERLOO BLACK HAWK CO	COUNTY CLINIC TRIBUNE PRESS BLDG	ALL	✓	✓	✓		
	KANSAS						
COLUMBUS CHEROKEE CO	COUNTY CLINIC	ALL	✓	✓	✓		

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** IN ADDITION TO CLINICS LISTED, THE ADDRESSES OF PHYSICIANS GIVING TREATMENT FOR VENEREAL DISEASES UNDER THE STATE PLAN MAY BE OBTAINED FROM STATE, COUNTY, AND MUNICIPAL OFFICERS.

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY	PAY
EMPORIA LYON CO	COUNTY CLINIC OR H C NUTTINGS OFC	ALL	✓	✓	✓		
HAYS ELLIS CO	COUNTY CLINIC OR P S BRAOYS OFFICE	ALL	✓	✓	✓		
HUTCHINSON RENO CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
JUNCTION CITY GEARY CO	COUNTY V O CLINIC OR C V MINNICKS OFC	ALL	✓	✓	✓		
KANSAS CITY WYANOOTTE CO	CITY HALL CLINIC 6TH AND ANN AVE	ALL	✓	✓	✓		
KANSAS CITY WYANOOTTE CO	UNIV OF KANSAS HOSP 39TH AND RAINBOW STS	ALL	✓	✓	✓	✓	✓
LAWRENCE DOUGLAS CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
LEAVENWORTH LEAVENWORTH CO	COUNTY CLINIC BROADWAY AT REESE ST	ALL	✓	✓	✓		
MANHATTAN RILEY CO	COUNTY HEALTH DEPT COUNTY COURTHOUSE	ALL	✓	✓	✓		
PARSONS LABETTE CO	COUNTY P H CLINIC 112 SOUTH 18TH ST	ALL	✓	✓	✓		
SALINA SALINA CO	COUNTY CLINIC 617 UNITED LIFE BLDG	ALL	✓	✓	✓		
TOPEKA SHAWNEE CO	CITY CLINIC CITY HALL	ALL	✓	✓	✓	✓	
WICHITA SEDGWICK CO	COUNTY CLINIC 300 S BROADWAY	ALL	✓	✓	✓		
	KENTUCKY						
ADAIRVILLE LOGAN CO	COUNTY CLINIC SQUARE	ALL	✓	✓	✓		
ALBANY CLINTON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓	✓	
ANCHORAGE JEFFERSON CO	GRIFFYTOWN CLINIC	ALL	✓	✓	✓		
ASHLAND BOYD CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
BARBOURVILLE KNOX CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
BARDWELL CARLISLE CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	✓
BEDFORD TRIMBLE CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
BENTON MARSHALL CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
BEREA MADISON CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
BOONEVILLE OWSLEY CO	CO HEALTH DEPT	ALL	✓	✓	✓		
BOWLING GREEN WARREN CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓	✓	
BRANDENBURG MEADE CO	CO HEALTH DEPT	ALL	✓	✓	✓		
BROOKSVILLE BRACKEN CO	CO HEALTH DEPT	ALL	✓	✓	✓		
BROWNSVILLE EDMONSON CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
BURKESVILLE CUMBERLAND CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
CADIZ TRIGG CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
CAMP TAYLOR JEFFERSON CO	CITY CLINIC 1430 LINCOLN ST	W	✓	✓	✓		
CAMPTON WOLFE CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
CARLISLE NICHOLAS CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
CARROLLTON CARROLL CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
CENTRAL CITY MUHLENBERG CO	COUNTY CLINIC CITY BLDG	ALL	✓	✓	✓	✓	
CLINTON HICKMAN CO	COUNTY HEALTH DEPT CLINTON BANK BLDG	ALL	✓	✓	✓		
COLUMBIA ADAIR CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
CORBIN WHITLEY CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
COVINGTON KENTON CO	COUNTY HEALTH DEPT 912 SCOTT ST	ALL	✓	✓	✓	✓	
CYNTHIANA HARRISON CO	CO HEALTH DEPT	ALL	✓	✓	✓		
DIXON WEBSTER CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
EDDYVILLE LYON CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
EDMONTON METCALFE CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
ELIZABETHTOWN HARDIN CO	COUNTY HEALTH DEPT 124 W DIXIE AVE	ALL	✓	✓	✓	✓	
ELKTON TODD CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
FLEMINGSBURG FLEMING CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
FREDONIA CALDWELL CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
FRENCHBURG MENIFEE CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		

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KENTUCKY

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
FULLERTON GREENUP CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
FULTON FULTON CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
GEORGETOWN SCOTT CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
GLASGOW BARREN CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
GRAYSON CARTER CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
GREENSBURG GREEN CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
GREENUP GREENUP CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
GREENVILLE MUHLENBERG CO	COUNTY HEALTH DEPT BAILEY BLDG	ALL	✓	✓	✓	✓	
HARDINSBURG BRECKINRIDGE CO	CO HEALTH DEPT	ALL	✓	✓	✓		
HARRODSBURG MERCER CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
HARTFORD OHIO CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
HAWESVILLE HANCOCK CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
HAZARD PERRY CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
HENDERSON HENDERSON CO	COUNTY HEALTH DEPT CITY BLDG	ALL	✓	✓	✓	✓	
HICKMAN FULTON CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
HINDMAN KNOTT CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
HOPKINSVILLE CHRISTIAN CO	CO HEALTH DEPT	ALL	✓	✓	✓		
HOPKINSVILLE CHRISTIAN CO	METHODIST CHURCH 2ND AND VIRGINIA STS	N	✓	✓	✓		
HORSE CAVE HART CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
HYDEN LESLIE CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
INEZ MARTIN CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
IRVINE ESTILL CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
JACKSON BREATHITT CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
LA CENTER BALLARD CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
LAWRENCEBURG ANDERSON CO	COUNTY HEALTH DEPT MAIN ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
LEITCHFIELD GRAYSON CO	CO HEALTH DEPT	ALL	✓	✓	✓		
LEXINGTON FAYETTE CO	COUNTY HEALTH DEPT 212 N UPPER ST	ALL	✓	✓	✓		
LEWISPORT HANCOCK CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
LIBERTY CASEY CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
LONDON LAUREL CO	COUNTY HEALTH DEPT MAIN ST	ALL	✓	✓	✓		
LOUISA LAWRENCE CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
LOUISVILLE JEFFERSON CO	CENTRAL CLINIC 920 W CHESTNUT ST	ALL	✓		✓	✓	
LOUISVILLE JEFFERSON CO	CITY HOSPITAL PRESTON CHESTNUT ST	ALL	✓	✓	✓	✓	
LOUISVILLE JEFFERSON CO	EAST CLINIC 1076 WASHINGTON ST	ALL	✓		✓	✓	
LOUISVILLE JEFFERSON CO	HIGHLAND PARK CLINIC CRITTENDEN HIAWATHA	ALL	✓		✓	✓	
LOUISVILLE JEFFERSON CO	COUNTY HEALTH DEPT FISCAL COURT BLDG	ALL	✓	✓	✓		
LOUISVILLE JEFFERSON CO	NEWBURG CLINIC ROUTE NO 1	N	✓	✓	✓		
LOUISVILLE JEFFERSON CO	PORTLAND CLINIC 2318 PORTLAND ST	ALL	✓		✓	✓	
MCKEE JACKSON CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
MADISONVILLE HOPKINS CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
MANCHESTER CLAY CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
MARION CRITTENDEN CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
MAYFIELD GRAVES CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
MAYSVILLE MASON CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
MIDDLESBORO BELL CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
MONTICELLO WAYNE CO	CO HEALTH DEPT	ALL	✓	✓	✓		
MOREHEAD ROWAN CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
MORGANFIELD UNION CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
MORGANTOWN BUTLER CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
MT VERNON ROCKCASTLE CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		

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KENTUCKY

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
MUNFOROVILLE HART CO	COUNTY HEALTH OEPT HEALTH OEPT OFFICE	ALL	✓	✓	✓		
MURRAY CALLOWAY CO	COUNTY HEALTH OEPT HEALTH OEPT OFFICE	ALL	✓	✓	✓		
NEWPORT CAMPBELL CO	COUNTY CLINIC 821 MONMOUTH ST	ALL	✓	✓	✓	✓	
OWENSBORO DAVIESS CO	CO HEALTH OEPT	ALL	✓	✓	✓		
OWENTON OWEN CO	COUNTY HEALTH OEPT HEALTH OEPT OFFICE	ALL	✓	✓	✓		
PAOUCAH MCCRACKEN CO	COUNTY HEALTH OEPT 524 N 4TH ST	ALL	✓	✓	✓	✓	
PAINTSVILLE JOHNSON CO	COUNTY HEALTH DEPT COURT ST	W	✓	✓	✓		
PARIS BOURBON CO	CO HEALTH DEPT	ALL	✓	✓	✓		
PIKESVILLE PIKE CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓	✓	
PINEVILLE BELL CO	COUNTY HEALTH OEPT HEALTH OEPT OFFICE	ALL	✓	✓	✓		
PRESTONSBURG FLOYO CO	COUNTY HEALTH OEPT COURT ST	ALL	✓	✓	✓		
PRINCETON CALOWELL CO	COUNTY HEALTH OEPT E MAIN ST	ALL	✓	✓	✓		
PROVIOENCE WEBSTER CO	CO V O CLINIC	ALL	✓	✓	✓		
RICHMONO MADISON CO	COUNTY HEALTH OEPT FEOERAL BLOG	ALL	✓	✓	✓	✓	
RUSSELL GREENUP CO	COUNTY HEALTH OEPT HEALTH OEPT OFFICE	ALL	✓	✓	✓		
RUSSELLVILLE LOGAN CO	COUNTY HEALTH OEPT N MAIN ST	ALL	✓	✓	✓		
SALEM LIVINGSTON CO	COUNTY HEALTH OEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
SASS RIOGE FULTON CO	COUNTY HEALTH OEPT HEALTH OEPT OFFICE	ALL	✓	✓	✓		
SCOTTSVILLE ALLEN CO	COUNTY HEALTH OEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
SMITHLANO LIVINGSTON CO	COUNTY HEALTH OEPT HEALTH OEPT OFFICE	ALL	✓	✓	✓		
SOMERSET PULASKI CO	COUNTY HEALTH OEPT HEALTH OEPT OFFICE	ALL	✓	✓	✓		
STANFORD LINCOLN CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
STANTON POWELL CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
STURGIS UNION CO	V D CLINIC REAR OF E M B A BLDG	ALL	✓	✓	✓		
TAYLORSVILLE SPENCER CO	COUNTY HEALTH OEPT MAIN ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
TOMPKINSVILLE MONROE CO	CO HEALTH DEPT	ALL	✓	✓	✓		
VALLEY STATION JEFFERSON CO	MEADOWLAWN H CENTER ROUTE NO 2	ALL	✓	✓	✓		
WARSAW GALLATIN CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
WEST LIBERTY MORGAN CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
WHITESBURG LETCHER CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
WHITLEY CITY MCCREARY CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
WICKLIFFE BALLARD CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
WILLIAMSBURG WHITLEY CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
WILLIAMSTOWN GRANT CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
YEADDISS LESLIE CO	COUNTY HEALTH DEPT HEALTH DEPT OFFICE	ALL	✓	✓	✓		
	LOUISIANA						
ABBEVILLE VERMILION CO	PARISH HEALTH UNIT WHITE STREET	ALL	✓	✓	✓		
ALEXANDRIA RAPIDES CO	PARISH HEALTH UNIT NEW COURTHOUSE	ALL		✓	✓		
ARCADIA BIENVILLE CO	PARISH HEALTH UNIT	ALL	✓		✓		
BASTROP MOREHOUSE CO	PARISH HEALTH UNIT 225 E MADISON ST	ALL	✓	✓	✓		
BATCHELOR POINTE COUPEE CO	PARISH HEALTH UNIT	ALL	✓		✓		
BATON ROUGE E BATON ROUGE CO	E BATON ROUGE CLINIC 101 NORTH BOULEVARD	ALL	✓	✓	✓		
BENTON BOSSIER CO	HEALTH CLINIC COURTHOUSE ANNEX	ALL	✓		✓		
BERMUDA NATCHITOCHES CO	CITY CLINIC	ALL	✓	✓	✓		
BERNICE UNION CO	PARISH HEALTH UNIT DR C COLVINS OFFICE	ALL	✓	✓	✓		
BOGALUSA WASHINGTON CO	HEALTH CENTER	ALL	✓		✓		
BONITA MOREHOUSE CO	HEALTH CLINIC DR OWENS OFFICE	ALL	✓	✓	✓		
BOSSIER CITY BOSSIER CO	V O CLINIC MINDEN STREET	ALL	✓	✓	✓		

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LOUISIANA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
BOYCE RAPIDES CO	HEALTH CENTER RAPIDES CO	ALL	✓	✓	✓		
CALHOUN OUACHITA CO	PARISH CLINIC MASONIC HOME	ALL	✓		✓		
CAMPTI NATCHITOCHES CO	CITY CLINIC POST OFFICE BLDG	ALL	✓	✓	✓		
CARENCRO LAFAYETTE CO	ASSUMPTION COL CLIN	N	✓	✓	✓		
CASPIANA CADDO CO	PARISH HEALTH UNIT COLORED LODGE BLDG	ALL	✓		✓		
CHURCH POINT ACADIA CO	PARISH CLINIC HOSPITAL STREET	ALL	✓	✓	✓		
CLARKS CALDWELL CO	HEALTH UNIT	ALL	✓	✓	✓		
COLFAX GRANT CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
COLLINSTON MOREHOUSE CO	PARISH CLINIC	ALL	✓	✓	✓		
COLUMBIA CALDWELL CO	HEALTH CLINIC	ALL	✓	✓	✓		
COTTON VALLEY WEBSTER CO	HEALTH CLINIC	ALL	✓	✓	✓		
COUSHATTA RED RIVER CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
COVINGTON ST TAMMANY CO	PARISH HEALTH UNIT SOUTHERN HOTEL BLDG	ALL	✓	✓	✓		
CROWLEY ACADIA CO	PARISH HEALTH UNIT 901 SO PARKERSON AVE	ALL	✓	✓	✓		
DE RIDDER BEAUREGARD CO	HEALTH CLINIC	ALL	✓	✓	✓		
DESTREHAN ST CHARLES CO	PARISH CLINIC PAN AM CLUBHOUSE	ALL	✓		✓		
DIXIE CADDO CO	CA SHREV HEALTH UNIT	ALL	✓		✓		
DONALDSONVILLE ASCENSION CO	PARISH HEALTH UNIT CHETENIACHES ST	ALL	✓	✓	✓		
DUPLESSIS ASCENSION CO	PARISH HEALTH UNIT K C HALL	ALL	✓	✓	✓		
EAST POINT RED RIVER CO	HEALTH CLINIC	ALL	✓	✓	✓		
ELIZABETH ALLEN CO	LUMBER CO HOSP	ALL	✓		✓		
ELTON JEFFERSON DAVIS	HEALTH CLINIC CITY HALL	ALL	✓	✓	✓		
EPPS WEST CARROLL CO	HEALTH CLINIC	ALL	✓		✓		
EPPS WEST CARROLL CO	HEALTH CLINIC HOLT MURPHY PLANTATN	ALL	✓		✓		
EVENING STAR CADDO CO	CA SHREV HEALTH UNIT	ALL	✓		✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
FARMERVILLE UNION CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
FERRIDAY CONCORDIA CO	HEALTH CLINIC OLD HWY PATROL OFC	ALL	✓	✓	✓		
FRANKLIN ST MARY CO	PARISH HEALTH CENTER REAR OF COURTHOUSE	ALL	✓		✓		
FRANKLINTON WASHINGTON CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
GILLIAM CADDO CO	CA SHREV HEALTH UNIT	ALL	✓		✓		
GLENMORA RAPIDES CO	HEALTH CLINIC SCHOOL HOUSE	ALL	✓	✓	✓		
GLOSTER DESOTO CO	PARISH CLINIC	ALL	✓	✓	✓		
GRAMBLING LINCOLN CO	NORMAL SCH CLINIC ADMINISTRATION BLOG	N	✓	✓	✓		
GRAND CANE DESOTO CO	PARISH CLINIC R 3 KINGSTON	ALL	✓	✓	✓		
GUEYDAN VERMILION CO	PARISH HEALTH UNIT MAIN STREET	ALL	✓		✓		
HAHNVILLE STCHARLES CO	PARISH HEALTH UNIT	ALL	✓		✓		
HAYNESVILLE CLAIBORNE CO	PARISH HEALTH UNIT	ALL	✓		✓		
HOLLY RIDGE RICHLAND CO	PARISH HEALTH UNIT OR CALHOUNS OFFICE	ALL	✓		✓		
HOMER CLAIBORNE CO	PARISH HEALTH UNIT	ALL	✓		✓		
HOUMA TERREBONNE CO	PARISH HEALTH UNIT 724 LAFAYETTE	ALL	✓		✓		
IOTA ACADIA CO	V D CLINIC EAST MAIN ST	ALL	✓	✓	✓		
JEANERETTE IBERIA CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
JENA LA SALLE CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
JENNINGS JEFFERSON DAVIS	PARISH HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		
JONESBORO JACKSON CO	PARISH CLINIC	ALL	✓	✓	✓		
JONESVILLE CATAHOULA CO	HEALTH CENTER	ALL	✓	✓	✓		
KAPLAN VERMILION CO	V D CLINIC	ALL	✓	✓	✓		
LAFAYETTE LAFAYETTE CO	CITY CHAHITY HOSP ST MARY ST	ALL	✓		✓		
LAFAYETTE LAFAYETTE CO	ST PAUL COLOREO CLIN ST JOHN AT SIMCOE ST	N	✓	✓	✓		
LAKE ARTHUR JEFFERSON DAVIS	PARISH HEALTH UNIT HOLLOWAY BLDG	ALL	✓	✓	✓		

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LOUISIANA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
LAKE PROVIDENCE EAST CARROLL CO	PARISH HEALTH UNIT OLD COURTHOUSE	ALL	✓	✓	✓		
LAKE ST JOHN CONCORDIA CO	PARISH HEALTH UNIT FORTY ACRE STORE	ALL	✓	✓	✓		
LECOMPTE RAPIDES CO	HEALTH CLINIC CITY HALL	ALL	✓	✓	✓		
LEESVILLE VERNON CO	PARISH HEALTH UNIT NEAR FIRE STATION	ALL	✓	✓	✓		
LIBERTY CADDO CO	PARISH HEALTH UNIT COLORED METH CHURCH	ALL	✓		✓		
LOCKPORT LA FOURCHE CO	HEALTH CLINIC OLD CITY HALL BLDG	ALL	✓	✓	✓		
LOUISA ST MARY CO	PARISH HEALTH CENTER ACROSS BAYOU FM STOR	ALL	✓		✓		
MADISONVILLE SAINT TAMMANY CO	CITY HOSP CLINIC	ALL	✓		✓		
MANSFIELD DESOTO CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
MANSFIELD DESOTO CO	KINGSTON V O CLINIC	ALL	✓	✓	✓		
MARINGOUIN IBERVILLE CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
MARKSVILLE AVOYELLES CO	PARISH HEALTH UNIT COURTHOUSE 2ND FLOOR	ALL	✓	✓	✓		
MELROSE NATCHITOCHES CO	CITY CLINIC	ALL	✓	✓	✓		
MERRYVILLE BEAUREGARD CO	HEALTH CLINIC CITY HALL	ALL	✓	✓	✓		
MINDEN WEBSTER CO	PARISH HEALTH UNIT	ALL	✓		✓		
MIRA CADDO CO	PARISH HEALTH UNIT	ALL	✓		✓		
MONROE OUACHITA CO	PARISH HEALTH UNIT OLD POST OFFICE BLDG	ALL	✓		✓		
MORGAN CITY ST MARY CO	PARISH HEALTH UNIT CITY HALL	ALL	✓		✓		
MOUNT OLIVE CADDO CO	PARISH HEALTH UNIT OVER CASKET FACTORY	ALL	✓		✓		
NATCHITOCHES NATCHITOCHES CO	PARISH HEALTH UNIT 206 POSTOFFICE BLDG	ALL	✓	✓	✓		
NEWELLTON TENSAS CO	PARISH HEALTH UNIT	ALL	✓		✓		
NEW IBERIA IBERIA CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
NEW ORLEANS ORLEANS CO	CHARITY HOSPITAL 1532 TULANE AVE	ALL	✓	✓	✓		
NEW ORLEANS ORLEANS CO	FLINT GOODRIDGE CLIN 2425 LOUISIANA AVE	N	✓	✓	✓		
NEW ORLEANS ORLEANS CO	HUTCHINSON MEM HOSP TULANE AVE	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
NEW ORLEANS ORLEANS CO	ISOLATION HOSP 513 N RAMPART ST	ALL	✓	✓	✓		
NEW ORLEANS ORLEANS CO	TOURO INFIRMARY 3516 PRYTANIA ST	ALL	✓	✓	✓	✓	
NEW ORLEANS ORLEANS CO	V D CONTROL DIVISION CITY HALL ANNEX	ALL	✓	✓	✓		
NEW ROADS POINTE COUPEE CO	PARISH HEALTH UNIT COURTHOUSE ANNEX	ALL	✓		✓		
OAKDALE ALLEN CO	PARISH HEALTH UNIT SOUTH TENTH ST	ALL	✓		✓		
OAK GROVE WEST CARROLL CO	PARISH HEALTH UNIT	ALL	✓		✓		
OAK RIDGE MOREHOUSE CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
OBERLIN ALLEN CO	PARISH HEALTH UNIT COURTHOUSE	ALL	✓		✓		
OPELOUSAS ST LANDRY CO	PARISH V D CLINIC COURTHOUSE ANNEX	ALL	✓	✓	✓		
PINEVILLE RAPIDES CO	LONG CHARITY HOSP	ALL	✓	✓	✓		
PLAQUEMINE IBERVILLE CO	PARISH HEALTH UNIT PLAQUEMINE COURT	ALL	✓		✓		
RAYNE ACADIA CO	HEALTH CLINIC 102 N CUNNINGHAM ST	ALL	✓	✓	✓		
RAYVILLE RICHLAND CO	CITY CLINIC	ALL	✓		✓		
RINGGOLD BIENVILLE CO	HEALTH CLINIC	ALL	✓		✓		
ROBSON CADDO CO	CA SHREV HEALTH UNIT	ALL	✓		✓		
RUSTON LINCOLN CO	PARISH HEALTH UNIT OLD HIGH SCHOOL	ALL	✓		✓		
ST JOSEPH TENSAS CO	PARISH HEALTH UNIT MASONIC LODGE	ALL	✓		✓		
ST MARTINVILLE ST MARTIN CO	PARISH HEALTH UNIT 201 COURTHOUSE BLDG	ALL	✓		✓		
SHREVEPORT CADDO CO	CA SHREV HEALTH UNIT MUNICIPAL AUDITORIUM	ALL	✓	✓	✓		
SICILY ISLAND CATAHOULA CO	CITY CLINIC	ALL	✓	✓	✓		
SONDHEIMER EAST CARROLL CO	CITY CLINIC STEVENS DRUG STORE	ALL	✓	✓	✓		
SPEARSVILLE UNION CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
SPRING HILL WEBSTER CO	PARISH HEALTH UNIT	ALL	✓		✓		
TALLULAH MADISON CO	CITY CLINIC COURTHOUSE	ALL	✓		✓		
THIBODAUX LA FOURCHE CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
VIDALIA CONCOROIA CO	PARISH HEALTH UNIT CITY HALL	ALL	✓	✓	✓		
VILLE PLATTE EVANGELINE CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
VIVIAN CADDO CO	CA SHREV HEALTH UNIT LIONS HALL	ALL	✓		✓		
WATERPROOF TENSAS CO	PARISH HEALTH UNIT	ALL	✓		✓		
WEEKS ISLAND IBERIA CO	PARISH HEALTH UNIT	ALL	✓	✓	✓		
WELSH JEFFERSON DAVIS	PARISH HEALTH UNIT KLEIMAN BLDG	ALL	✓	✓	✓		
WHITE CASTLE IBERVILLE CO	PARISH HEALTH UNIT	ALL	✓		✓		
WINNFIELD WINN CO	PARISH HEALTH UNIT PHOENIX DRUG STORE	ALL	✓	✓	✓		
WINNSBORO FRANKLIN CO	PARISH HEALTH UNIT	ALL	✓		✓		
WINNSBORO FRANKLIN CO	MT ZION CLINIC	ALL	✓	✓	✓		
WISNER FRANKLIN CO	PARISH HEALTH UNIT	ALL	✓		✓		
	MAINE						
AUGUSTA KENNEBEC CO	STATE V D CLINIC 283 WATER ST RM 2	ALL	✓	✓	✓		
BANGOR PENOBSCOT CO	STATE V D CLINIC 162 FRENCH ST	ALL	✓	✓	✓	✓	✓
BATH SAGADOHOC CO	STATE V D CLINIC CUSTOM HOUSE	ALL	✓	✓	✓		
BELFAST WALDO CO	STATE V D CLINIC 5 NORTHPORT AVE	ALL	✓	✓		✓	
BIDDEFORD YORK CO	STATE V D CLINIC WEBBER HOSP	ALL	✓	✓	✓		
BINGHAM SOMERSET CO	STATE V D CLINIC	ALL	✓	✓	✓		
CALAIS WASHINGTON CO	STATE V D CLINIC CALAIS HOSP	ALL	✓	✓		✓	
DANFORTH WASHINGTON CO	STATE V D CLINIC	ALL	✓	✓	✓		✓
EASTPORT WASHINGTON CO	STATE V D CLINIC	ALL	✓	✓	✓		
ELLSWORTH HANCOCK CO	STATE V D CLINIC 75 MAIN ST	ALL	✓	✓	✓		
GRAND ISLE AROOSTOOK CO	STATE V D CLINIC	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
GUILFORD PISCATAQUIS CO	STATE V D CLINIC	ALL	✓	✓	✓		
HOULTON AROOSTOOK CO	STATE V D CLINIC MASONIC BLDG	ALL	✓	✓		✓	
ISLAND FALLS AROOSTOOK CO	STATE V D CLINIC	ALL	✓	✓	✓	✓	✓
KITTERY YORK CO	STATE V D CLINIC 28 WENTWORTH ST	ALL	✓	✓	✓		
LEWISTON ANDROSCOGGIN CO	STATE V D CLINIC ST MARYS HOSP	ALL	✓	✓	✓		
LEWISTON ANDROSCOGGIN CO	STATE V D CLINIC 198 LISBON ST	ALL	✓	✓	✓		
MILLINOCKET PENOBSCOT CO	STATE V D CLINIC 3 HIGHLAND AVE	ALL	✓	✓	✓	✓	
OLD TOWN PENOBSCOT CO	STATE V D CLINIC 197 CENTRE ST	ALL	✓	✓	✓	✓	
PORTLAND CUMBERLAND CO	STATE V D CLINIC MAINE GENERAL HOSP	ALL	✓	✓	✓		
PORTLAND CUMBERLAND CO	STATE V D CLINIC 65 INDIA ST	ALL	✓	✓		✓	
PORTLAND CUMBERLAND CO	STATE V D CLINIC M EYE EAR INFIRMARY	ALL	✓	✓	✓		
PRESQUE ISLE AROOSTOOK CO	STATE V D CLINIC MAIN STREET	ALL	✓	✓	✓		
ROCKLAND KNOX CO	STATE V D CLINIC 407 MAIN ST	ALL	✓	✓	✓		
RUMFORD OXFORD CO	STATE V D CLINIC 5 FRANKLIN ST	ALL	✓	✓	✓	✓	
SANFORD YORK CO	STATE V D CLINIC 29 WINTER ST	ALL	✓	✓	✓		
WATERVILLE KENNEBEC CO	STATE V D CLINIC SISTERS HOSPITAL	ALL	✓	✓	✓		
WILTON FRANKLIN CO	STATE V D CLINIC MAIN STREET	ALL	✓	✓	✓		
WINTHROP KENNEBEC CO	STATE V D CLINIC 1 WESTERN AVE	ALL	✓	✓	✓		
	MARYLAND						
ANNAPOLIS ANNE ARUNDEL CO	V D CLINIC OLD HIGH SCHOOL BLDG	ALL	✓	✓	✓		
ANNAPOLIS ANNE ARUNDEL CO	ST MARGARETS CLINIC R F D NO 2	ALL	✓	✓	✓		
BALTIMORE	EYE EAR THROAT HOSP EUTAW AND LANVALE	ALL	✓			✓	
BALTIMORE	CITY CLINIC NO 1 MUNICIPAL BLDG	A	✓	✓	✓		

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MARYLAND

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
BALTIMORE	CITY CLINIC NO 2 1313 ORUID HILL AVE	NM	✓	✓	✓		
BALTIMORE	CITY CLINIC NO 3 28 SOUTH BROADWAY	WM	✓	✓	✓		
BALTIMORE	CITY CLINIC NO 4 419 N BOND ST	NM	✓	✓	✓		
BALTIMORE	CITY CLINIC NO 5 1313 DRUID HILL AVE	NF	✓		✓		
BALTIMORE	CITY CLINIC NO 6 1313 DRUID HILL AVE	N	✓		✓		
BALTIMORE	CITY CLINIC NO 7 1313 DRUID HILL AVE	N M	✓		✓		
BALTIMORE	GOOD SHEPHERD CLINIC MOUNT AND HOLLINS ST	F W	✓	✓	✓		
BALTIMORE	JOHNS HOPKINS HOSP BROADWAY AT MONUMENT	ALL	✓			✓	
BALTIMORE	GU DISP JNO HOPKINS BROADWAY AT MONUMENT	M		✓		✓	
BALTIMORE	MERCY HOSPITAL CALVERT AND SARATOGA	A	✓	✓			✓
BALTIMORE	ST AGNES HOSPITAL CATON AND WILKINS	WM	✓	✓			✓
BALTIMORE	SINAI HOSPITAL MONUMENT AND RUTLAND	W	✓	✓		✓	✓
BALTIMORE	S BALTIMORE GEN HOSP LIGHT STREET	ALL	✓	✓			✓
BALTIMORE	W BALTIMORE GEN HOSP RAYNOR AND OUKELAND	W	✓	✓			✓
BEL AIR HARFORD CO	STATE CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
BERLIN WORCESTER CO	STATE CLINIC HEALTH CENTER BLDG	ALL	✓	✓	✓		
BRUNSWICK FREDERICK CO	STATE CLINIC B AND O EMERG HOSP	ALL	✓	✓	✓		
CAMBRIDGE DORCHESTER CO	STATE CLINIC CAMBRIDGE MD HOSP	ALL	✓	✓	✓		
CENTERVILLE QUEEN ANNE CO	STATE CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CHESTERTOWN KENT CO	STATE CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CRISFIELD SOMERSET CO	STATE CLINIC HEALTH CENTER BLDG	ALL	✓	✓	✓		
CUMBERLAND ALLEGANY CO	STATE CLINIC CITY HALL	ALL	✓	✓	✓		
DAMASCUS MONTGOMERY CO	STATE CLINIC NEW ELEMENTARY SCH	ALL	✓	✓	✓		
DAWSONVILLE MONTGOMERY CO	STATE CLINIC OR U O NOURSES OFC	ALL	✓	✓	✓		
DENTON CAROLINE CO	STATE CLINIC HEALTH OFFICE	ALL	✓	✓	✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
EASTON TALBOT CO	STATE CLINIC COUNTY HEALTH OEPT	ALL	✓	✓	✓		
ELDERSBURG CARROLL CO	OR LAWSONS OFFICE	ALL	✓	✓	✓		
ELKTON CECIL CO	OOCTORS OFFICE EAST HIGH ST	ALL	✓	✓	✓		
ELLICOTT CITY HOWARO CO	STATE CLINIC COUNTY HEALTH OEPT	ALL	✓	✓	✓		
FEOERALSBURG CAROLINE CO	STATE CLINIC HEALTH CENTER	ALL	✓	✓	✓		
FREOERICK FREDERICK CO	STATE CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
GRAYTON CHARLES CO	STATE CLINIC CHURCH HALL	ALL	✓	✓	✓		
HAGERSTOWN WASHINGTON CO	STATE CLINIC COUNTY HEALTH OEPT	ALL	✓	✓	✓		
HAVRE OE GRACE HARFORO CO	STATE CLINIC CO HEALTH CENTER	ALL	✓	✓	✓		
HUGHESVILLE CHARLES CO	STATE CLINIC DR CHAPPELEARS OFC	ALL	✓	✓	✓		
HURLOCK OORCHESTER CO	STATE CLINIC BANK MAIN AT POPLAR	ALL	✓	✓	✓		
HYATTSVILLE PRINCE GEORGES CO	STATE CLINIC COUNTY SERVICE BLOG	ALL	✓	✓	✓		
KITZMILLER GARRETT CO	STATE CLINIC DR R R SISSONS OFC	ALL	✓	✓	✓		
LA PLATA CHARLES CO	STATE CLINIC COUNTY HEALTH OEPT	ALL	✓	✓	✓		
LAUREL PRINCE GEORGES CO	STATE CLINIC POLICE COURT BLOG	ALL	✓	✓	✓		
LEONARDTOWN ST MARYS CO	STATE CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
LINDEN MONTGOMERY CO	STATE CLINIC COLORED SCHOOL	ALL	✓	✓	✓		
MC KENDREE ANNE ARUNDEL CO	V D CLINIC POLLING HOUSE	ALL	✓	✓	✓		
MAGOTHY ANN ARUNDEL CO	HEALTH CENTER	ALL	✓	✓	✓		
NORBECK MONTGOMERY CO	HEALTH CENTER						
OAKLAND GARRETT CO	STATE CLINIC DR BAUMGARTNER OFC	ALL	✓	✓	✓		
PASADENA ANNE ARUNDEL CO	STATE CLINIC HEALTH CENTER	ALL	✓	✓	✓		
POCOMOKE CITY WORCESTER CO	CLINIC CENTER FIFTH STREET	ALL	✓	✓	✓		
POMONKEY CHARLES CO	STATE CLINIC ELKS HALL	ALL	✓	✓	✓		
PRINCE FREDERICK CALVERT CO	STATE CLINIC COUNTY HOSPITAL	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
PRINCESS ANNE SOMERSET CO	STATE CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
ROCKVILLE MONTGOMERY CO	STATE CLINIC COURTHOUSE	ALL	✓	✓	✓		
SALISBURY WICOMICO CO	DR FISHERS CLINIC CHURCH AT N DIVISION	ALL	✓	✓			✓
SALISBURY WICOMICO CO	COUNTY HEALTH DEPT WATSON MEMORIAL BLDG	ALL	✓	✓	✓		
SANDY SPRING MONTGOMERY CO	V D CLINIC COLORED SCHOOL	ALL	✓	✓	✓		
SNOW HILL WORCESTER CO	STATE CLINIC ODD FELLOWS BLDG	ALL	✓	✓	✓		
SPARROWS POINT BALTIMORE CO	STATE CLINIC BETHLEHEM STEEL HOSP	ALL	✓	✓	✓		
STEVENSVILLE QUEEN ANNES CO	STATE CLINIC GROLLMANS BLDG	ALL	✓	✓	✓		
SUDLERSVILLE QUEEN ANNES CO	STATE CLINIC REDDEN RESIDENCE	ALL	✓	✓	✓		
TOWSON BALTIMORE CO	STATE CLINIC HEALTH DEPT BLDG	ALL	✓	✓	✓		
UPPER MARLBORO PRINCE GEORGES CO	STATE CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
WESTERNPORT ALLEGANY CO	STATE CLINIC REEVES HOSPITAL	ALL	✓	✓	✓		
WESTMINSTER CARROLL CO	STATE CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
WHEATON MONTGOMERY CO	STATE CLINIC DR SEWELLS OFFICE	ALL	✓	✓	✓		
	MASSACHUSETTS						
BEVERLY ESSEX CO	BEVERLY HOSPITAL HERRICK AT HEATHER	ALL	✓	✓	✓	✓	✓
BOSTON SUFFOLK CO	BETH ISRAEL HOSP 330 BROOKLINE AVE	ALL	✓	✓	✓	✓	✓
BOSTON SUFFOLK CO	BOSTON CITY HOSPITAL 818 HARRISON AVE	ALL	✓	✓	✓	✓	✓
BOSTON SUFFOLK CO	BOSTON DISPENSARY 25 BENNET ST	ALL	✓	✓	✓	✓	✓
BOSTON SUFFOLK CO	CHILDRENS HOSPITAL 300 LONGWOOD AVE	C	✓		✓	✓	✓
BOSTON SUFFOLK CO	MASS GENERAL HOSP FRUIT ST	ALL	✓	✓	✓	✓	✓
BOSTON SUFFOLK CO	MASS MEMORIAL HOSP 88 EAST CONCORD ST	ALL	✓	✓	✓	✓	✓
BOSTON SUFFOLK CO	P B BRIGHAM HOSPITAL 721 HUNTINGTON AVE	ALL	✓	✓	✓	✓	✓

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
BROCKTON PLYMOUTH CO	BROCKTON HOSPITAL 680 CENTER ST	ALL	✓	✓	✓	✓	✓
CAMBRIDGE MIDDLESEX CO	CAMBRIDGE CITY HOSP 1493 CAMBRIDGE ST	ALL	✓	✓	✓		
CAMBRIDGE MIDDLESEX CO	CAMBRIDGE HOSPITAL 330 MOUNT AUBURN ST	ALL	✓		✓	✓	✓
FALL RIVER BRISTOL CO	BD OF HEALTH CLINIC CITY HALL ANNEX	ALL	✓	✓	✓	✓	✓
FITCHBURG WORCESTER CO	BURBANK HOSPITAL HOSPITAL ROAD	ALL	✓	✓	✓	✓	✓
GREAT BARRINGTON BERKSHIRE CO	FAIRVIEW HOSPITAL LEWIS AVE	ALL	✓	✓	✓	✓	✓
HAVERHILL ESSEX CO	BD OF HEALTH CLINIC 471 MAIN ST	ALL	✓	✓	✓	✓	✓
HOLYOKE HAMPSHIRE CO	HOLYOKE HOSPITAL BEECH ST	ALL	✓	✓	✓	✓	✓
LAWRENCE ESSEX CO	BD OF HEALTH CLINIC 130 OAK ST	ALL	✓	✓	✓	✓	✓
LAWRENCE ESSEX CO	CITY CLINIC 133 METHUEN ST	ALL	✓	✓	✓	✓	✓
LOWELL MIDDLESEX CO	BD OF HEALTH CLINIC KIRK AND PAIGE STS	ALL	✓	✓	✓	✓	✓
LYNN ESSEX CO	LYNN HOSPITAL 212 BOSTON ST	ALL	✓	✓	✓	✓	✓
NEW BEDFORD BRISTOL CO	BD OF HEALTH CLINIC 519 OLYMPIA BLDG	ALL	✓	✓	✓	✓	✓
NEWTON MIDDLESEX CO	NEWTON HOSPITAL 2014 WASHINGTON ST	ALL	✓	✓	✓	✓	✓
PITTSFIELD BERKSHIRE CO	HOUSE OF MERCY HOSP 741 NORTH ST	ALL	✓	✓	✓	✓	✓
QUINCY NORFOLK CO	QUINCY DISP CLINIC HIGH SCHOOL AVE	ALL	✓	✓	✓		
ROXBURY SUFFOLK CO	N E HOSP FOR WOMEN DIMOCK STREET	F C	✓	✓	✓	✓	✓
SPRINGFIELD HAMPSHIRE CO	SPRINGFIELD HOSPITAL 759 CHESTNUT ST	ALL	✓	✓	✓	✓	✓
WALTHAM MIDDLESEX CO	WALTHAM HOSPITAL HOPE AVE	ALL	✓		✓	✓	✓
WORCESTER WORCESTER CO	MEMORIAL HOSPITAL 119 BELMONT ST	ALL	✓	✓	✓	✓	✓
WORCESTER WORCESTER CO	WORCESTER CITY HOSP 162 CHANDLER ST	ALL	✓	✓	✓	✓	✓
	MICHIGAN						
BATTLE CREEK CALHOUN CO	COUNTY CLINIC ROOM NO 8 CITY HALL	ALL	✓	✓	✓		

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MICHIGAN

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
BENTON HARBOR BERRIEN CO	COUNTY CLINIC	ALL	✓	✓	✓		
BERRIEN CENTER BERRIEN CO	COUNTY CLINIC	ALL	✓	✓	✓		
DEARBORN WAYNE CO	MEDICAL CENTER 10149 MICHIGAN AVE	ALL	✓	✓	✓		
DETROIT WAYNE CO	DEACONESS HOSPITAL 3245 E JEFFERSON AVE	ALL	✓	✓	✓	✓	
DETROIT WAYNE CO	GRACE HOSPITAL 268 E WILLIS AVE	ALL	✓	✓	✓	✓	✓
DETROIT WAYNE CO	HARPER HOSPITAL 3825 BRUSH ST	A	✓	✓	✓		✓
DETROIT WAYNE CO	NORTH END CLINIC 936 HOLBROOK ST	ALL	✓	✓	✓	✓	
DETROIT WAYNE CO	SOCIAL HYG CLINIC 555 CLINTON ST	ALL	✓	✓	✓		
ELOISE WAYNE CO	ELOISE HOSP CLINIC	ALL	✓	✓	✓	✓	
FLINT GENESEE CO	HEALTH DEPT CLINIC HURLEY HOSPITAL	ALL	✓	✓	✓		
GRAND RAPIDS KENT CO	SOCIAL HYG CLINIC CITY HALL	ALL	✓	✓	✓		
HAMTRAMCK WAYNE CO	COUNTY CLINIC 10036 JOS CAMPAU AVE	ALL	✓	✓	✓		
HIGHLAND PARK WAYNE CO	GENERAL HOSPITAL	ALL	✓	✓	✓		
JACKSON JACKSON CO	CITY DIAG CLINIC CITY OFFICES	ALL	✓	✓	✓		
KALAMAZOO KALAMAZOO CO	CITY CLINIC 241 W SOUTH ST	ALL	✓	✓	✓		
LANSING INGHAM CO	CITY CLINIC 112 W ALLEGAN ST	ALL	✓	✓	✓		
MIDLAND MIDLAND CO	HEALTH DEPT CLINIC COUNTY HEALTH OFFICE	W	✓	✓	✓		
PONTIAC OAKLAND CO	CITY DIAG CLINIC 465 W HURON ST	ALL	✓	✓	✓		
PONTIAC OAKLAND CO	COUNTY CLINIC 436 AUBURN AVE	ALL	✓	✓	✓		
RIVER ROUGE WAYNE CO	SUMBY MEMORIAL HOSP 600 PALMERSTONE	ALL	✓	✓		✓	✓
ROYAL OAK OAKLAND CO	CITY CLINIC 111 S TROY ST	ALL	✓	✓	✓		
SAGINAW SAGINAW CO	CITY CLINIC 130 E BRISTOL ST	ALL	✓	✓	✓		
WYANDOTTE WAYNE CO	CITY HEALTH CLINIC 839 BIDDLE AVE	W	✓	✓	✓		
YPSILANTI WASHTENAW CO	SOCIAL HYG CLINIC CITY HALL	ALL	✓		✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TD *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
	MINNESOTA						
DULUTH ST LOUIS CO	V D CLINIC HEARDING HOSPITAL	ALL	✓	✓	✓		
MINNEAPOLIS HENNEPIN CO	LYMANHURST HLTH CEN 1800 CHICAGO AVE	ALL	✓	✓	✓		
MINNEAPOLIS HENNEPIN CO	MINNEAPOLIS GEN HOSP 619 S 5TH ST	ALL	✓	✓	✓		
MINNEAPOLIS HENNEPIN CO	MINNESOTA GENERAL UNIV HOSPITALS	ALL	✓	✓	✓	✓	
MINNEAPOLIS HENNEPIN CO	WELLS MEMORIAL 75 GLENWOOD AVE N	ALL	✓	✓		✓	
ROCHESTER OLMSTED CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
ST PAUL RAMSEY CO	AMHERST WILDER DISP 279 RICE ST	ALL	✓	✓		✓	
ST PAUL RAMSEY CO	ANCKER HOSPITAL COLBOURNE AT JEFFRSN	ALL	✓	✓	✓		
SAVAGE SCOTT CO	STATE TRANSIENT CAMP V D CLINIC CAMP NO 3	M	✓	✓	✓		
	MISSISSIPPI						
ABBEVILLE LAFAYETTE CO	COUNTY CLINIC	ALL	✓	✓	✓		
ABERDEEN MONROE CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
ALLIGATOR BOLIVAR CO	V D CLINIC CLINIC BUILDING	ALL	✓	✓	✓		
AMORY MONROE CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
ANGUILLA SHARKEY CO	COUNTY CLINIC DR H B GOODMANS OFC	ALL	✓	✓	✓		
ARCOLA WASHINGTON CO	COUNTY V D CLINIC	ALL	✓	✓	✓		
ARTESIA LOWNDES CO	COUNTY CLINIC HILLS DRUG STORE	ALL	✓	✓	✓		
ASHLAND BENTON CO	V D CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
BALDWYN LEE CO	V D CLINIC DR R B CALDWELLS OFC	ALL	✓	✓	✓		
BASSFIELD JEFFERSON DAVIS	V D CLINIC CITY RECREATION CEN	ALL	✓	✓	✓		
BATESVILLE PANOLA CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
BAY SPRINGS JASPER CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
BELMONT TISHOMINGO CO	V D CLINIC COMMUNITY STORE	ALL	✓	✓	✓		
BELZONI HUMPHREYS CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
BENTON YAZOO CO	COUNTY CLINIC DR S H WOODS OFFICE	ALL	✓	✓	✓		
BENTONIA YAZOO CO	COUNTY CLINIC DR J V JAMES OFFICE	ALL	✓	✓	✓		
BOONEVILLE PRENTISS CO	V U CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
BRANDON RANKIN CO	COUNTY CLINIC HEALTH DEPT	ALL	✓	✓	✓		
BROOKHAVEN LINCOLN CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
BROOKVILLE NOXUBEE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CALEDONIA LOWNDES CO	V D CLINIC DARRACOTTS BLDG	ALL	✓	✓	✓		
CAMDEN MADISON CO	COUNTY CLINIC DR J W MELVINS OFC	ALL	✓	✓	✓		
CANTON MADISON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CARY SHARKEY CO	HEALTH CENTER	ALL	✓	✓	✓		
CATCHINGS SHARKEY CO	COUNTY HLTH CENTER	ALL	✓	✓	✓		
CHARLESTON TALLAHATCHIE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CLARKSDALE COAHOMA CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
CLARKSDALE COAHOMA CO	COUNTY CLINIC KING ANDERSON PLANT	ALL	✓	✓	✓		
CLEVELAND BOLIVAR CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
COLDWATER TATE CO	COUNTY CLINIC ABOVE ELDERS STORE	ALL	✓	✓	✓		
COLLINS COVINGTON CO	V D CLINIC POST OFFICE BLDG	ALL	✓	✓	✓		
COLLINSVILLE LAUDERDALE CO	V D CLINIC DR WILLIAMS OFFICE	ALL	✓	✓	✓		
COLUMBIA MARION CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
COLUMBUS LOWNDES CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
COMO PANOLA CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CORINTH ALCORN CO	COUNTY HEALTH DEPT FRANKLIN ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
CRAWFORD LOWNDES CO	V D CLINIC FRAZIERS DRUG STORE	ALL	✓	✓	✓		
CRENSHAW PANOLA CO	COUNTY CLINIC	ALL	✓	✓	✓		
CRUGER HOLMES CO	COUNTY HEALTH DEPT MAIN ST	ALL	✓	✓	✓		
OEESON BOLIVAR CO	COUNTY CLINIC BULL PEN	ALL	✓	✓	✓		
OEKALB KEMPER CO	COUNTY HEALTH OEPT	ALL	✓	✓	✓		
OOOOSVILLE SUNFLOWER CO	COUNTY CLINIC COLEMANS WAREHOUSE	ALL	✓	✓	✓		
OREW SUNFLOWER CO	COUNTY CLINIC COLOREO CHURCH	ALL	✓	✓	✓		
OUBBS TUNICA CO	COUNTY CLINIC PERRYS COMMISSARY	ALL	✓	✓	✓		
OUBLIN COAHOMA CO	COUNTY CLINIC OR C Z BALLAROS OFC	ALL	✓	✓	✓		
OUNOEE TUNICA CO	COUNTY CLINIC HERRINCS STORE	ALL	✓	✓	✓		
EBENEZER HOLMES CO	COUNTY CLINIC ROUTE 4	ALL	✓	✓	✓		
EDWARDS HINDS CO	COUNTY CLINIC C D NOBLE BLDG	ALL	✓	✓	✓		
ELLISVILLE JONES CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
EVANSVILLE TUNICA CO	COUNTY CLINIC OWENS COMMISSARY	ALL	✓	✓	✓		
FITLER ISSAQUENA CO	COUNTY HEALTH OEPT HEALTH CENTER	ALL	✓	✓	✓		
FLORA MAOISON CO	COUNTY HEALTH OEPT	ALL	✓	✓	✓		
FOUR MILE HUMPHREYS CO	COUNTY CLINIC SCHOOL BUILOINC	ALL	✓	✓	✓		
FRIARS POINT COAHOMA CO	COUNTY HEALTH OEPT OLO COURTHOUSE	ALL	✓	✓	✓		
CEORCETOWN COPIAH CO	COUNTY HEALTH OEPT TOWN HALL BLOC	ALL	✓	✓	✓		
CLEN ALLEN WASHINCTON CO	COUNTY HEALTH DEPT CLINIC BLOG	ALL	✓	✓	✓		
CLENOORA TALLAHATCHIE CO	COUNTY HEALTH OEPT	ALL	✓	✓	✓		
CLOSTER AMITE CO	COUNTY HEALTH OEPT TOWN HALL	ALL	✓	✓	✓		
CRACE ISSAQUENA CO	COUNTY HEALTH OEPT WHITAKERS STORE	ALL	✓	✓	✓		
GREENVILLE WASHINCTON CO	COUNTY HEALTH OEPT NORTH HARVEY ST	ALL	✓	✓	✓		
CREENWOOO LEFLORE CO	COUNTY HEALTH OEPT	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
GUNNISON BOLIVAR CO	COUNTY HEALTH DEPT OLD BANK BLDG	ALL	✓	✓	✓		
HATTIESBURG FORREST CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
HAZELHURST COPIAH CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
HEIDELBERG JASPER CO	V D CLINIC	ALL	✓	✓	✓		
HERNANDO DE SOTO CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
HOLLANDALE WASHINGTON CO	COUNTY HEALTH DEPT CLINIC BLDG	ALL	✓	✓	✓		
HOLLY BLUFF YAZOO CO	COUNTY CLINIC DR H C OWENS OFFICE	ALL	✓	✓	✓		
HOLLY SPRINGS MARSHALL CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
HUSHPUCKENA BOLIVAR CO	V D CLINIC OLD SERVICE STATION	ALL	✓	✓	✓		
INDIANOLA SUNFLOWER CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
INVERNESS SUNFLOWER CO	COUNTY HEALTH DEPT COLORED SCHOOL	ALL	✓	✓	✓		
ISOLA HUMPHREYS CO	COUNTY HEALTH DEPT MAYORS OFFICE	ALL	✓	✓	✓		
ITTA BENA LEFLORE CO	COUNTY HEALTH DEPT ROUTE 2	ALL	✓	✓	✓		
IUKA TISHOMINGO CO	COUNTY CLINIC	ALL	✓	✓	✓		
JACKSON HINUS CO	COUNTY HEALTH UEPT COURTHOUSE BUILOING	ALL	✓	✓	✓		
JONESTOWN COAHOMA CO	COUNTY HEALTH DEPT CITY LIBRARY	ALL	✓	✓	✓		
LAKE CORMORANT DE SOTO CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
LAUUERDALE LAUDERDALE CO	COUNTY HEALTH DEPT DR MCKINNONS OFFICE	ALL	✓	✓	✓		
LAUREL JONES CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
LEAKESVILLE GREENE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
LELANO WASHINGTON CO	COUNTY HEALTH DEPT CLINIC BLDG	ALL	✓	✓	✓		
LIBERTY AMITE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
LOMBAROY SUNFLOWER CO	COUNTY HEALTH DEPT COLORED CHURCH	ALL	✓	✓	✓		
LOUISE HUMPHREYS CO	COUNTY HEALTH DEPT DR MECKLINS OFFICE	ALL	✓	✓	✓		
LUCEDALE GEORGE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
LULA COAHOMA CO	COUNTY HEALTH DEPT THE LIBRARY	ALL	✓	✓	✓		
MC COMB PIKE CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓	✓	✓		
MACON NOXUBEE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
MADISON MADISON CO	HEALTH CENTER	ALL	✓	✓	✓		
MAGEE SIMPSON CO	CITY CLINIC	ALL	✓	✓	✓		
MAGNOLIA PIKE CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓	✓	✓		
MARIANNA MARSHALL CO	COUNTY CLINIC OLO SCHOOL BLDG	ALL	✓	✓	✓		
MAYERSVILLE ISSAQUENA CO	COUNTY CLINIC COLORED CHURCH	ALL	✓	✓	✓		
MENDENHALL SIMPSON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
MERIDIAN LAUDERDALE CO	COUNTY HEALTH DEPT 1319 23RD AVE	ALL	✓	✓	✓		
MERIGOLD BOLIVAR CO	COUNTY HEALTH DEPT PARK BLDG	ALL	✓	✓	✓		
MIDWAY YAZOO CO	V D CLINIC	ALL	✓	✓	✓		
MILESTON HOLMES CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
MILLARD PEARL CO	COUNTY CLINIC BATSONS STORE	ALL	✓	✓	✓		
MINTER CITY LEFLORE CO	COUNTY HEALTH DEPT CLINIC BLDG	ALL	✓	✓	✓		
MONEY LEFLORE CO	COUNTY HEALTH DEPT COLORED SCHOOL	ALL	✓	✓	✓		
MONTICELLO LAWRENCE CO	V D CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
MOORHEAD SUNFLOWER CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
MOUNT OLIVE COVINGTON CO	V D CLINIC	ALL	✓	✓	✓		
MOUNT PLEASANT MARSHALL CO	V D CLINIC DR C C CONNERS OFC	ALL	✓	✓	✓		
MYRTLE UNION CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
NATCHEZ ADAMS CO	COUNTY HEALTH DEPT MUNICIPAL BLDG	ALL	✓	✓	✓		
NETTLETON LEE CO	COUNTY HEALTH DEPT DR J T DABBS OFFICE	ALL	✓	✓	✓		
NEW ALBANY UNION CO	COUNTY HEALTH DEPT 305 MAIN ST	ALL	✓	✓	✓		
NEW AUGUSTA PERRY CO	HEALTH CLINIC	ALL	✓	✓	✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
NEWHEBRON LAWRENCE CO	V D CLINIC OR IZARUS OFFICE	ALL	✓	✓	✓		
NITTA YUMA SHARKEY CO	COUNTY HEALTH DEPT CASTLEBERRYS STORE	ALL	✓	✓	✓		
OLIVE BRANCH DE SOTO CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
OSYKA PIKE CO	CITY SYPHILIS CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
OXFORD LAFAYETTE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
PACE BOLIVAR CO	COUNTY HEALTH DEPT WOLF BLDG	ALL	✓	✓	✓		
PAULETTE NOXUBEE CO	COUNTY HEALTH DEPT COLORED SCHOOL	ALL	✓	✓	✓		
PICAYUNE PEARL RIVER CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
PINOLA SIMPSON CO	COUNTY V D CLINIC SCHOOL GYM	ALL	✓	✓	✓		
PLANTERSVILLE LEE CO	COUNTY HEALTH DEPT OR CANTRELLS OFFICE	ALL	✓	✓	✓		
POPLARVILLE PEARL RIVER CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
PORT GIBSON CLAIBORNE CO	V D CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
PRENTISS JEFFERSON DAVIS	V D CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
QUITMAN CLARKE CO	V D CLINIC COMMUNITY HOUSE	ALL	✓	✓	✓		
RALEIGH SMITH CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
RIPLEY TIPPAH CO	V D CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
ROBINSONVILLE TUNICA CO	COUNTY HEALTH DEPT SCHOOL BLDG	ALL	✓	✓	✓		
ROLLING FORK SHARKEY CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
ROME SUNFLOWER CO	V D CLINIC STILLIONS STORE	ALL	✓	✓	✓		
RUSEDALE BOLIVAR CO	COUNTY HEALTH DEPT OLU POST OFFICE	ALL	✓	✓	✓		
ROUNDAWAY COAHOMA CO	COUNTY HEALTH DEPT KYLE PLANTATION	ALL	✓	✓	✓		
RULEVILLE SUNFLOWER CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SARDIS PANOLA CO	HEALTH CLINIC	ALL	✓	✓	✓		
SATARTIA YAZOO CO	V D CLINIC	ALL	✓	✓	✓		
SCOUBA KEMPER CO	COUNTY CLINIC MAYORS OFFICE	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
SCOTT BOLIVAR CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SENATOBIA TATE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SHANNON LEE CO	COUNTY HEALTH DEPT DR COWDENS OFFICE	ALL	✓	✓	✓		
SHAW BOLIVAR CO	COUNTY HEALTH DEPT W P A LIBRARY	ALL	✓	✓	✓		
SHELBY BOLIVAR CO	COUNTY HEALTH DEPT OLD CAFE	ALL	✓	✓	✓		
SHELLMOUND LEFLORE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SHERARD COAHOMA CO	COUNTY HEALTH DEPT	N	✓	✓	✓		
SHUBUTA CLARKE CO	V D CLINIC BANK BUILDING	ALL	✓	✓	✓		
SHUQUALAK NOXUBEE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SILVER CITY HUMPHREYS CO	COUNTY HEALTH DEPT DR G S BRYANS OFFICE	ALL	✓	✓	✓		
SKENE BOLIVAR CO	V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
SUMNER TALLAHATCHIE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SUNFLOWER SUNFLOWER CO	COUNTY HEALTH DEPT DR B H HIGDONS OFC	ALL	✓	✓	✓		
TAYLOR LAFAYETTE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
TAYLORSVILLE SMITH CO	V D CLINIC AINSWORTH HOTEL	ALL	✓	✓	✓		
TCHULA HOLMES CO	HEALTH CLINIC	ALL	✓	✓	✓		
THORNTON HOLMES CO	V D CLINIC	ALL	✓	✓	✓		
THYATIRA TATE CO	COUNTY HEALTH DEPT HYDES STORE	ALL	✓	✓	✓		
TUNICA TUNICA CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
TUPELO LEE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
VICKSBURG WARREN CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
WALLS DE SOTO CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
WAYNESBORO WAYNE CO	V D CLINIC OLD OFC CHANCERY CLK	ALL	✓	✓	✓		
WESSON COPIAH CO	COUNTY HEALTH DEPT HERMAN BLDG	ALL	✓	✓	✓		
WIGGINS STONE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
YAZOO CITY YAZOO CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
	MISSOURI						
AURORA LAWRENCE CO	SW MO V D CLINIC CITY HALL	ALL	✓	✓	✓		
AVA DOUGLAS CO	COUNTY V D CLINIC	ALL	✓	✓		✓	
BUTLER BATES CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
CAMERON CLINTON CO	CITY CLINIC	ALL	✓	✓	✓		
CANTON LEWIS CO	V D CLINIC DR JENNINGS OFFICE	ALL	✓	✓	✓		
CAPE GIRARDEAU CAPE GIRARDEAU CO	V D CLINIC SPANISH AND BROADWAY	ALL	✓	✓	✓		
CARTHAGE JASPER CO	SW MO V D CLINIC BENTON SCHOOL	ALL	✓	✓	✓		
CARUTHERSVILLE PEMISCOT CO	COUNTY CLINIC	ALL	✓	✓	✓		
CASSVILLE BARRY CO	CO HOSP V D CLINIC BARRY COUNTY HOSP	ALL	✓	✓	✓		
CHARLESTON MISSISSIPPI CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
CLAYTON ST LOUIS CO	V D CLINIC	ALL	✓	✓	✓		
CLINTON HENRY CO	COUNTY CLINIC COUNTY COURTHOUSE	ALL	✓	✓	✓		
DE SOTO JEFFERSON CO	HEALTH CLINIC 112 A N MAIN ST	ALL	✓		✓		
DEXTER STODDARD CO	CITY CLINIC	ALL	✓	✓	✓		
DONIPHAN RIPLEY CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
EAST PRAIRIE MISSISSIPPI CO	V D CLINIC MOBILE	ALL	✓	✓	✓		
ELDON MILLER CO	DR SHELTONS CLINIC 6 S MAPLE ST	ALL	✓	✓		✓	
FAYETTE HOWARD CO	LEE HOSPITAL	ALL	✓	✓	✓		
FREDERICKTOWN MADISON CO	SYPHILIS CLINIC 126 WEST MAIN ST	ALL	✓	✓	✓		
FULTON CALLAWAY CO	V D CLINIC COURTHOUSE	ALL	✓		✓		
HANNIBAL MARION CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE	CLINIC TREATS		FEE SYSTEM		
		TD *	SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
HARRISONVILLE CASS CO	V D CLINIC 106A EAST PEARL ST	ALL	✓	✓	✓		
HIGGINSVILLE LAFAYETTE CO	PUBLIC HEALTH CLINIC RUSSELL AND PATRICK	ALL	✓	✓	✓		
HOUSTON TEXAS CO	COUNTY V D CLINIC	ALL	✓	✓	✓		
INDEPENDENCE JACKSON CO	CITY V D CLINIC 100 WEST MAPLE ST	N	✓	✓	✓		
JEFFERSON CITY COLE CO	V D CLINIC 234 MADISON ST	ALL	✓		✓		
JOPLIN JASPER CO	SW MO V D CLINIC CITY HALL	ALL	✓	✓	✓		
KANSAS CITY JACKSON CO	ALFRED BENJAMIN DISP 1000 ADMIRAL BLVD	ALL	✓	✓	✓	✓	
KANSAS CITY JACKSON CO	CHILDRENS MERCY HOSP 1710 INDEPENDENCE AV	WC	✓		✓		
KANSAS CITY JACKSON CO	GENERAL HOSPITAL NO2 600 EAST 22ND ST	N	✓	✓	✓		
KANSAS CITY JACKSON CO	GENERAL HOSPITAL NO1 24TH AND CHERRY STS	W	✓	✓	✓		
KANSAS CITY JACKSON CO	GOOD SHEPHERD CLINIC 6724 TROOST	FC	✓	✓	✓		
KANSAS CITY JACKSON CO	HELPING HAND INST 13 EAST MISSOURI AVE	WCM	✓	✓	✓		
KANSAS CITY JACKSON CO	MUNICIPAL T B HOSP LEEDS STATION	ALL	✓		✓		
KANSAS CITY JACKSON CO	CABOT CLUB CLINIC 721 WEST 18TH ST	ALL	✓	✓		✓	
KANSAS CITY JACKSON CO	WHEATLEY HOSPITAL 1826 FOREST AVE	N	✓	✓		✓	
KENNETT DUNKLIN CO	V D CLINIC	ALL	✓	✓	✓		
KOCH ST LOUIS CO	ROBERT KOCH HOSP	ALL	✓	✓	✓		
LEBANON LACLEDE CO	V D CLINIC COUNTY COURTHOUSE	ALL	✓	✓	✓		
LITTLE BLUE JACKSON CO	JACKSON CO HOSPITAL	W	✓	✓	✓		
LOUISIANA PIKE CO	COUNTY V D CLINIC PIKE CO HOSPITAL	ALL	✓	✓	✓		
MALDEN DUNKLIN CO	V D CLINIC	ALL	✓	✓	✓		
MARCELINE LINN CO	CITY CLINIC EAST HOWELL ST	ALL	✓	✓	✓		
MEXICO AUDRAIN CO	CITY CLINIC 101 N WESTERN ST	ALL	✓	✓	✓		
MOBERLY RANDOLPH CO	V D CLINIC NURSES OFFICE	ALL	✓	✓	✓		
MONETT BARRY CO	V D CLINIC DISTRICT HEALTH OFC	ALL	✓	✓	✓		

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MISSOURI

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
MT LEVEL	HEALTH CLINIC MT LEVEL PLANTATION	ALL	✓	✓	✓		
MT VERNON LAWRENCE CO	SW MO V D CLINIC COUNTY COURTHOUSE	ALL	✓	✓	✓		
NEDSHO NEWTON CO	SW MO V D CLINIC SOCIAL SECURITY BLDG	ALL	✓	✓	✓		
NEW MADRID NEW MADRID CO	COUNTY CLINIC	ALL	✓		✓		
OSCEOLA ST CLAIR CO	V D CLINIC PUBLIC HEALTH OFFICE	ALL	✓	✓	✓		
OWENSVILLE GASCONADE CO	HEALTH OFFICE CLINIC	W	✓	✓	✓		
PALMYRA MARION CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
PLATTE CITY PLATTE CO	COUNTY CLINIC CO HEALTH DEPT	ALL	✓	✓	✓		
PLEASANT HILL CASE CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
POPLAR BLUFF BUTLER CO	V D CLINIC COUNTY COURTHOUSE	ALL	✓	✓	✓		
PORTAGEVILLE NEW MADRID CO	CITY CLINIC	ALL	✓		✓		
RICHMOND RAY CO	CO V D CLINIC DR T F COOKS OFFICE	ALL	✓	✓	✓		
ROLLA PHELPS CO	COUNTY V D CLINIC STATE TRACHOMA HOSP	ALL	✓	✓	✓		
ST JOSEPH BUCHANAN CO	V D CLINIC COMMUNITY HALL	ALL	✓	✓	✓		
ST LOUIS ST LOUIS CO	ALEXIAN BROS HOSP 3933 SOUTH BROADWAY	W	✓	✓	✓		
ST LOUIS ST LOUIS CO	CITY HOSPITAL NO 1 14TH AT LAFAYETTE ST	ALL	✓	✓	✓		
ST LOUIS ST LOUIS CO	CITY ISOLATION HOSP 5600 ARSENAL ST	ALL	✓		✓	✓	
ST LOUIS ST LOUIS CO	CITY SPECIAL HOSP 4200 SOUTH BROADWAY	F	✓	✓	✓		
ST LOUIS ST LOUIS CO	GOOD SHEPHERD CONV 3801 GRAVOIS ST	W	✓	✓	✓		
ST LOUIS ST LOUIS CO	FIRMIN DESLOGE HOSP 1325 S GRAND ST	ALL	✓	✓	✓	✓	
ST LOUIS ST LOUIS CO	H G PHILLIPS HOSP 2601 N WHITTIER ST	N	✓	✓	✓		
ST LOUIS ST LOUIS CO	JEWISH HOSPITAL 216 S KINGSHIGHWAY	W	✓	✓	✓	✓	✓
ST LOUIS ST LOUIS CO	V D DIAG CLINIC 18 MUNICIPAL CT BLDG	ALL	✓	✓	✓		
ST LOUIS ST LOUIS CO	ST JOHNS DISPENSARY 4945 AUBUDON AVE	W	✓	✓	✓	✓	✓
ST LOUIS ST LOUIS CO	ST MARYS INFIRMARY 1536 PAPIN ST	N	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
ST LOUIS ST LOUIS CO	WASHINGTON U CLINICS 507 S EUCLID AVE	ALL	✓	✓		✓	
SALEM DENT CO	V D CLINIC OLD COMMUNITY BLDG	ALL	✓	✓	✓		
SEDALIA PETTIS CO	PUBLIC HEALTH CLINIC 5TH AND LAMINE STS	ALL	✓	✓	✓		
SIKESTON SCOTT CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
SPRINGFIELD GREENE CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
STEELVILLE CRAWFORD CO	CRAWFORD CLINIC	ALL	✓	✓	✓		
THOMPSONS BEND MISSISSIPPI CO	V D CLINIC MOBILE	ALL	✓	✓	✓		
TRENTON GRUNDY CO	V D CLINIC 905 MAIN ST	ALL	✓	✓	✓		
TUSCUMBIA MILLER CO	HEALTH DEPT CLINIC COURTHOUSE	ALL	✓	✓	✓		
WARRENSBURG JOHNSON CO	PUBLIC HEALTH CLINIC 217 N HOLDEN ST	ALL	✓	✓	✓		
WARSAW BENTON CO	V D CLINIC DR J A LOGANS OFFICE	ALL	✓	✓	✓		
WASHINGTON FRANKLIN CO	COMMUNITY CLINIC 115 ELM ST	ALL	✓	✓	✓		
WAYNESVILLE PULASKI CO	V D CLINIC COUNTY HEALTH CENTER	ALL	✓	✓	✓		
WEBB CITY JASPER CO	COUNTY HEALTH DEPT 115 N MADISON ST	ALL	✓	✓	✓		
WOLF ISLAND MISSISSIPPI CO	V D CLINIC MOBILE	ALL	✓	✓	✓		
WYATT MISSISSIPPI CO	V D CLINIC MOBILE	ALL	✓	✓	✓		
	MONTANA						
BOZEMAN GALLATIN CO	CITY CO H OFFICE COURTHOUSE	ALL	✓	✓	✓		
GREAT FALLS CASCADE CO	CITY CO HEALTH DEPT CIVIC CENTER BLDG	ALL	✓	✓	✓		
	NEBRASKA **						
LINCOLN LANCASTER CO	CITY CLINIC 935 R ST	ALL	✓	✓	✓		

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** IN ADDITION TO CLINICS LISTED, THE ADDRESSES OF PHYSICIANS GIVING TREATMENT FOR VENEREAL DISEASES UNDER THE STATE PLAN MAY BE OBTAINED FROM STATE, COUNTY, AND MUNICIPAL OFFICERS.

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
OMAHA DOUGLAS CO	NORTH SIDE CLINIC AMER LEGION N030 BLG	ALL	✓	✓	✓		
OMAHA DOUGLAS CO	V D CLINIC 912 DOUGLAS ST	ALL	✓	✓	✓		
OMAHA DOUGLAS CO	CREIGHTON MED DISP 14TH AT DAVENPORT ST	ALL	✓	✓	✓		
OMAHA DOUGLAS CO	DOUGLAS CO HOSPITAL 40TH AT POPPLETON ST	ALL	✓	✓	✓		
OMAHA DOUGLAS CO	SOUTH SIDE CLINIC 24TH AND O STREETS	ALL	✓	✓	✓		
OMAHA DOUGLAS CO	U OF NEBR DISPENSARY 42ND ST AT DEWEY AVE	ALL	✓	✓	✓		
	NEVADA						
RENO WASHOE CO	V D CLINIC WASHOE GENERAL HOSP	ALL	✓	✓		✓	
	NEW HAMPSHIRE						
BERLIN COOS CO	ST LOUIS HOSP CLINIC 459 MAIN ST	ALL	✓	✓	✓		
CONCORD MERRIMACK CO	V D CLINIC 5 WARREN ST	ALL	✓	✓	✓		
DOVER STRAFFORD CO	V D CLINIC 90 WASHINGTON ST	ALL	✓	✓	✓		
MANCHESTER HILLSBORO CO	ELLIOT HOSP CLIN OP 955 AUBURN ST	ALL	✓	✓	✓		
NASHUA HILLSBORO CO	V D CLINIC 184 MAIN ST	ALL	✓	✓	✓		
PORTSMOUTH ROCKINGHAM CO	V D CLINIC PORTSMOUTH HOSPITAL	ALL	✓	✓	✓		
	NEW JERSEY						
ASBURY PARK MONMOUTH CO	SHORE REGION CLINIC 109 ATKINS AVE	ALL	✓		✓		
ATLANTIC CITY ATLANTIC CO	MUNICIPAL HOSPITAL 900 ADRIATIC AVE	ALL	✓	✓	✓		
BAYONNE HUDSON CO	BAYONNE HOSPITAL EAST 30TH ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
BELVIDERE WARREN CO	DR MARLETTS OFFICE 230 GREENWICH ST	ALL	✓		✓		
BLAIRSTOWN WARREN CO	DR BOSTWICKS OFFICE MAIN STREET	ALL	✓		✓		
BLOOMFIELD ESSEX CO	CITY HEALTH DEPT MUNICIPAL BLDG	ALL	✓	✓	✓		
BOONTON MORRIS CO	REGIONAL CLINIC 311 W MAIN ST	ALL	✓	✓	✓		
BORDENTOWN BURLINGTON CO	V D CLINIC 412 FARNSWORTH AVE	ALL	✓	✓	✓		
BOUND BROOK SOMERSET CO	BOUND BROOK HOSPITAL 507 CHURCH ST	ALL	✓	✓	✓		
BRANCHVILLE SUSSEX CO	DR LUSHEARS OFFICE MAIN STREET	ALL	✓		✓		
BRIDGETON CUMBERLAND CO	BRIDGETON HOSPITAL IRVING AVE	ALL	✓	✓	✓		
BURLINGTON BURLINGTON CO	DIST V D CLINIC CITY HALL HIGH ST	ALL	✓	✓	✓		
CAMDEN CAMDEN CO	COOPER HOSPITAL 6TH AND STEVENS STS	ALL	✓	✓	✓	✓	
CAMDEN CAMDEN CO	W JERSEY HOMEO HOSP ATLANTIC AVE	ALL	✓	✓	✓	✓	
CARTERET MIDDLESEX CO	DR KEMENYS OFFICE 48 PULASKI AVE	ALL	✓	✓	✓		
CRANBURY MIDDLESEX CO	V D CLINIC OLD HIGHTSTOWN RD	ALL	✓		✓		
DOVER MORRIS CO	HEALTH CLINIC 29 E BLACKWELL ST	ALL	✓	✓	✓		
EATONTOWN MONMOUTH CO	HEALTH CENTER SOUTH STREET	N	✓		✓		
ELIZABETH UNION CO	ALEXIAN BROS HOSP 655 EAST JERSEY ST	ALL	✓	✓	✓		
ELIZABETH UNION CO	ELIZABETH GEN HOSP REID AT E JERSEY	ALL	✓	✓	✓		
ELIZABETH UNION CO	ST ELIZABETH HOSP 204 S BROAD ST	ALL	✓	✓	✓		
ENGLEWOOD BERGEN CO	ENGLEWOOD HOSPITAL ENGLE STREET	ALL	✓	✓	✓		
EWING TP MERCER CO	V D CLINIC 1871 PENNINGTON RD	ALL	✓	✓	✓		
FRANKLIN SUSSEX CO	DR DRAKES OFFICE 47 MAIN STREET	ALL	✓		✓		
FREEHOLD MONMOUTH CO	COUNTY JAIL CLINIC COURTHOUSE	A	✓		✓		
FREEHOLD MONMOUTH CO	MCOSS HEALTH CENTER LAFAYETTE PLACE	ALL	✓		✓		
HACKENSACK BERGEN CO	HACKENSACK HOSPITAL HOSPITAL PLACE	ALL	✓	✓	✓	✓	
HACKETTSTOWN WARREN CO	DR MAXWELLS OFFICE 117 GRAND AVE	ALL	✓		✓		

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NEW JERSEY

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
HAMMONTON ATLANTIC CO	REGIONAL HEALTH COMM 108 BELLEVUE AVE	ALL	✓	✓	✓		
HIGHTSTOWN MERCER CO	V O CLINIC MAIN ST FIREHOUSE	ALL	✓	✓	✓		
IRVINGTON ESSEX CO	GENERAL HOSPITAL 832 CHANCELLOR AVE	ALL	✓	✓	✓		
JERSEY CITY HUDSON CO	CHRIST HOSPITAL 176 PALISADE AVE	ALL	✓	✓	✓	✓	
JERSEY CITY HUDSON CO	MEDICAL CENTER MONTGOMERY ST	ALL	✓	✓	✓	✓	
JERSEY CITY HUDSON CO	HAGUE MATERNITY HOSP CLIFTON PLACE	F	✓	✓	✓		
KEARNY HUDSON CO	OR R K HARVEYS OFC 711 KEARNY AVE	ALL	✓	✓	✓		
KEYPORT MONMOUTH CO	HEALTH CENTER 8 MAIN STREET	ALL	✓		✓		
LONG BRANCH MONMOUTH CO	MONMOUTH MEM HOSP 3RD AVE	ALL	✓	✓		✓	
LONG BRANCH MONMOUTH CO	HEALTH CENTER 65 FOURTH AVE	ALL	✓		✓		
MADISON MORRIS CO	REGIONAL HEALTH COMM 1 MADISON AVE	ALL	✓	✓		✓	
MAHWAH BERGEN CO	HEALTH CENTER HOHOKUS TOWNSHIP	ALL	✓		✓		
MANASQUAN MONMOUTH CO	HEALTH CENTER 67 MAIN ST	ALL	✓		✓		
MAYS LANDING ATLANTIC CO	REGIONAL HEALTH COMM COURTHOUSE	ALL	✓		✓		
MAYS LANDING ATLANTIC CO	ATLANTIC COUNTY JAIL	ALL	✓		✓		
MILLVILLE CUMBERLAND CO	CITY CLINIC 228 N 2ND ST	ALL	✓	✓	✓		
MONTCLAIR ESSEX CO	MOUNTAINSIDE HOSP BAY AVE	ALL	✓	✓	✓	✓	✓
MOORESTOWN BURLINGTON CO	COMMUNITY HOUSE 16 E MAIN ST	ALL	✓	✓	✓		
MORRISTOWN MORRIS CO	MEMORIAL HOSPITAL 66 MORRIS ST	ALL	✓	✓		✓	
MORRISTOWN MORRIS CO	REG TREATM CENTER WATER ST	ALL	✓	✓	✓		
MOUNT HOLLY BURLINGTON CO	BURLINGTON CO HOSP 175 MADISON	ALL	✓	✓	✓		
NEPTUNE MONMOUTH CO	FITKIN MEMORIAL HOSP CORLIES AVENUE	ALL	✓	✓	✓	✓	
NEWARK ESSEX CO	AMER LEGION HOSP BWAY AND GRAFTON	ALL	✓	✓	✓		
NEWARK ESSEX CO	COMMUNITY HOSPITAL 138 W KINNEY ST	W	✓	✓	✓	✓	
NEWARK ESSEX CO	HEALTH DEPT CLINIC ARLINGTON AT WILLIAM	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
NEWARK ESSEX CO	BETH ISRAEL HOSP 201 LYONS AVE	ALL	✓	✓	✓	✓	✓
NEW BRUNSWICK MIDDLESEX CO	MIDDLESEX GEN HOSP SOMERSET ST	ALL	✓	✓	✓		
NEW MONMOUTH MONMOUTH CO	MIDDLETOWN H CENTER CAMPBELLS JUNCTION	ALL	✓	✓	✓		
NEWTON SUSSEX CO	DR E HAWKES OFFICE 113 MAIN ST	ALL	✓		✓		
NORTHFIELD ATLANTIC CO	ATLANTIC CO HOSPITAL DOLPHIN AND SHORE	ALL	✓	✓	✓		
NORTH WILDWOOD CAPE MAY CO	DR MACES HOSP CLINIC 2410 ATLANTIC AVE	ALL	✓	✓	✓		
NUTLEY ESSEX CO	HEALTH DEPT 226 CHESTNUT ST	ALL	✓	✓	✓		
OGDENSBURG SUSSEX CO	DR AITKENS OFFICE	ALL	✓		✓		
ORANGE ESSEX CO	ORANGE MEMORIAL HOSP 188 S ESSEX AVE	ALL	✓	✓	✓		
PASSAIC PASSAIC CO	BETH ISRAEL HOSP 141 MADISON ST	ALL	✓	✓	✓	✓	
PASSAIC PASSAIC CO	GENERAL HOSPITAL LAFAYETTE AVE	ALL	✓	✓	✓		
PASSAIC PASSAIC CO	ST MARYS HOSPITAL 211 PENNINGTON AVE	ALL	✓	✓	✓		
PATERSON PASSAIC CO	BARNERT MEM HOSP 30TH ST AND BROADWAY	ALL	✓	✓	✓	✓	✓
PATERSON PASSAIC CO	BOARD OF HEALTH MILL AND PASSAIC STS	ALL	✓	✓	✓		
PATERSON PASSAIC CO	PATERSON GEN HOSP MARKET AND MADISON	ALL	✓	✓	✓		✓
PATERSON PASSAIC CO	ST JOSEPHS HOSP 703 MAIN ST	ALL	✓	✓	✓	✓	
PENNS GROVE SALEM CO	V D CLINIC OLD MOOSE HALL	ALL	✓	✓	✓		
PHILLIPSBURG WARREN CO	WARREN HOSPITAL 845 WILBUR AVE	ALL	✓	✓	✓		
PLAINFIELD UNION CO	MUHLENBERG HOSPITAL PARK AVE AT RANDOLPH	ALL	✓	✓	✓	✓	
PORT NORRIS TUMBERLAND CO	SHELL PILE CLINIC PLANTERS PACKING CO	ALL	✓		✓		
PRINCETON MERCER CO	PRINCETON HOSPITAL WITHERSPOON ST	ALL	✓	✓	✓		
RED BANK MONMOUTH CO	DR LORENZOS OFFICE 31 OAKLAND ST	W	✓		✓		
RED BANK MONMOUTH CO	M C O S S 131 PEARL ST	W	✓		✓		
RIVERSIDE BURLINGTON CO	ZURBRUGG MEM HOSP TAYLOR STREET	ALL	✓	✓	✓		
ROSELLE UNION CO	BOARD OF HEALTH 227 E NINTH	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
SALEM SALEM CO	CO MEMORIAL HOSPITAL NEW MARKET ST	ALL	✓	✓	✓		
SOMERS POINT ATLANTIC CO	SHORE MEMORIAL HOSP SUNNY AND N Y AVES	ALL	✓	✓	✓		
SOMERVILLE SOMERSET CO	SOMERSET HOSPITAL REHILL AVE	ALL	✓	✓	✓		✓
SPARTA SUSSEX CO	DR LONGNECKERS OFC WOODPORT ROAD	ALL	✓	✓	✓		
SUMMIT UNION CO	BOARD OF HEALTH 71 SUMMIT AVE	ALL	✓	✓	✓		
SUSSEX SUSSEX CO	DR L R EDDYS OFFICE 40 BANK ST	ALL	✓	✓	✓		
TEANECK BERGEN CO	HOLY NAME HOSPITAL TEANECK RD	ALL	✓	✓	✓	✓	
TRENTON MERCER CO	MCKINLEY MEM HOSP BRUNSWICK AVE	ALL	✓	✓	✓	✓	
TRENTON MERCER CO	HEALTH DEPT MUNICIPAL BUILDING	ALL	✓	✓	✓		
VINELAND CUMBERLAND CO	NEWCOMB HOSPITAL SOUTH STATE ST	ALL	✓	✓	✓		
WASHINGTON WARREN CO	DR VARNEYS OFFICE 122 BELVIDERE AVE	ALL	✓		✓		
WEEHAWKEN HUDSON CO	NORTH HUDSON HOSP PARK AVE	ALL	✓	✓	✓	✓	
WOODBINE CAPE MAY CO	STATE COLONY HOSP OE HIRSCH AVE	ALL	✓	✓	✓		
WOODBURY GLOUCESTER CO	UNDERWOOD HOSPITAL BROAD AND RED BANK	ALL	✓	✓	✓		
	NEW MEXICO						
ALAMOGORDO OTERO CO	V D TREATMENT CENTER DR J T LOWRYS OFFICE	ALL	✓	✓	✓		
ALBUQUERQUE BERNALILLO CO	CITY V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
ARTESIA EDDY CO	COUNTY CLINIC MEMORIAL HOSP	ALL	✓	✓	✓		
BELEN VALENCIA CO	CITY V D CLINIC W P A BUILDING	ALL	✓	✓	✓		
BERNALILLO SANDOVAL CO	V D CLINIC CO HEALTH DEPT	ALL	✓	✓	✓		
CARLSBAD EDDY CO	V D CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CLAYTON UNION CO	COUNTY V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
CLOVIS CURRY CO	CITY V D CLINIC COURTHOUSE	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
DEMING LUNA CO	CITY V D CLINIC COURTHOUSE BLDG	ALL	✓	✓	✓		
ESPANOLA RIO ARRIBA CO	V D CLINIC H DEPT BRANCH OFFC	ALL	✓	✓	✓		
FARMINGTON SAN JUAN CO	V D TREATMENT CENTER DR M D MORANS OFFICE	ALL	✓	✓	✓		
FORT SUMNER OE BACA CO	V O TREATMENT CENTER DR RUMINSONS OFFICE	ALL	✓	✓	✓		
GALLUP MCKINLEY CO	CITY V O CLINIC CO HEALTH OEPT	ALL	✓	✓	✓		
HOBBS LEE CO	V O CLINIC CITY HALL	ALL	✓	✓	✓		
LAS CRUCES ODNA ANA CO	V D TREATMENT CENTER DR DAVIETS OFFICE	ALL	✓	✓	✓		
LAS VEGAS SAN MIGUEL CO	CITY V O CLINIC RDMERO BLOCK	ALL	✓	✓	✓		
LORDSBURG HIDALGO CO	CITY V O CLINIC COURTHOUSE BLDG	ALL	✓	✓	✓		
LOS LUNAS VALENCIA CO	CITY V D CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
LOVINGTON LEA CO	COUNTY V O CLINIC CO COURTHOUSE	ALL	✓	✓	✓		
PECOS SAN MIGUEL CO	V O CLINIC HLTH OEPT BRANCH OFC	ALL	✓	✓	✓		
PORTALES RODSEVELT CO	V D TREATMENT CENTER 622 S W STATE	ALL	✓	✓	✓		
RATON COLFAX CO	CITY V O CLINIC CDUNTY COURTHOUSE	ALL	✓	✓	✓		
SANTA FE SANTA FE CO	CATHOLIC CLINIC CATHEDRAL PLACE	ALL	✓	✓	✓		
SILVER CITY GRANT CO	CITY V D CLINIC COUNTY COURTHOUSE	ALL	✓	✓	✓		
SOCORRO SOCORRO CO	TREATMENT CENTER DR BARTELS OFFICE	ALL	✓	✓	✓		
TUCUMCARI QUAY CO	V D TREATMENT CENTER DR WARNERS OFFICE	ALL	✓	✓	✓		
	NEW YORK						
ALBANY ALBANY CO	ALBANY HOSPITAL NEW SCOTLAND AVE	ALL	✓	✓	✓	✓	
ALBANY ALBANY CO	MEMORIAL HOSPITAL 714 BROADWAY	ALL	✓	✓	✓	✓	
ALBANY ALBANY CO	ST PETERS HOSPITAL NEW SCOTLAND AVE	ALL	✓	✓	✓		
AMSTERDAM MONTGOMERY CO	CITY CLINIC CITY HALL	ALL	✓	✓	✓		

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NEW YORK

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
AUBURN CAYUGA CO	SOCIAL HYGIENE CLIN AUBURN CITY HOSPITAL	ALL	✓	✓	✓		
BATH STEUBEN CO	BATH MEMORIAL HOSP 115 E STEUBEN ST	ALL	✓	✓	✓		
BEACON DUTCHESS CO	CITY SYPHILIS CLINIC 453 MAIN STREET	ALL	✓	✓	✓		
BINGHAMTON BROOME CO	HEALTH DEPT CLINIC 71 COLLIER ST	ALL	✓	✓	✓		
BROOKLYN KINGS CO	BETH MOSES HOSPITAL 404 HART ST	ALL	✓	✓		✓	
BROOKLYN KINGS CO	EYE AND EAR HOSP 29 GREENE AVE	ALL	✓		✓	✓	
BROOKLYN KINGS CO	BROOKLYN HOSPITAL DE KALB AND ASHLAND	ALL	✓	✓		✓	
BROOKLYN KINGS CO	BUSHWICK H CENTER 186 GROVE ST	ALL	✓	✓	✓		
BROOKLYN KINGS CO	CUMBERLAND HOSPITAL 39 AUBURN PLACE	C	✓		✓		
BROOKLYN KINGS CO	FT GREENE SOC HYG CL 295 FLATBUSH AVE EXT	ALL	✓	✓	✓		
BROOKLYN KINGS CO	GREENPOINT HOSPITAL KINGSLAND AVE	ALL	✓	✓	✓		
BROOKLYN KINGS CO	HARBOR HOSPITAL CROPSEY AND BAY 32ND	ALL	✓	✓		✓	
BROOKLYN KINGS CO	ISRAEL ZION HOSPITAL 4802 10TH AVE	ALL	✓			✓	
BROOKLYN KINGS CO	JEWISH HOSPITAL OPD 555 PROSPECT PLACE	ALL	✓	✓		✓	
BROOKLYN KINGS CO	KINGS CO HOSPITAL 451 CLARKSON AVE	ALL	✓	✓	✓		
BROOKLYN KINGS CO	LONG ISLANU COLL HOS PACIFIC AND AMITY	ALL	✓	✓		✓	
BROOKLYN KINGS CO	LUTHERAN HOSPITAL E N Y AVE AT JUNIUS	ALL	✓	✓		✓	
BROOKLYN KINGS CO	METHODIST HOSPITAL 6TH ST AND 7TH AVE	ALL		✓		✓	
BROOKLYN KINGS CO	OCEAN HILL MEM HOSP 343 RALPH AVE	ALL	✓	✓		✓	
BROOKLYN KINGS CO	RED HOOK GOWANUS CL 250 BALTIC ST	ALL	✓	✓	✓		
BROOKLYN KINGS CO	ST JOHNS HOSPITAL 480 HERKIMER ST	C	✓		✓	✓	
BROOKLYN KINGS CO	WMSBURG GREENPT CL 151 MAUJER ST	ALL	✓	✓	✓		
BUFFALO ERIE CO	BUFFALO COLUM HOSP 298 NIAGRA ST	ALL	✓	✓	✓	✓	
BUFFALO ERIE CO	BUFFALO GENERAL HOSP 100 HIGH ST	ALL	✓			✓	
BUFFALO ERIE CO	CHILDRENS HOSPITAL 219 BRYANT ST	ALL	✓		✓	✓	

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
BUFFALO ERIE CO	MEYER MEMORIAL HOSP 462 GRIDER ST	ALL	✓			✓	
BUFFALO ERIE CO	M FILLMORE HOSPITAL 875 LAFAYETTE AVE	A	✓	✓	✓		
BUFFALO ERIE CO	SWAN STREET CLINIC 175 SWAN ST	ALL	✓		✓	✓	
CAMBRIDGE WASHINGTON CO	MARY MCCLELLAN HOSP	ALL	✓	✓	✓		
CAMILLUS ONONDAGA CO	CITY CLINIC	ALL	✓	✓	✓		
CANASTOTA MADISON CO	PHYSICIANS OFFICE 129 PETERBORO ST	ALL	✓	✓	✓		
COBLESKILL SCHOHARIE CO	PHYSICIANS OFFICES	ALL	✓	✓	✓		
COEYMANS ALBANY CO	PHYSICIANS OFFICE CHURCH STREET	ALL	✓	✓	✓	✓	
COHOES ALBANY CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
CORNING STEUBEN CO	CITY CLINIC CITY HALL	ALL	✓	✓	✓		
CORTLAND CORTLAND CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
DUNKIRK CHAUTAUQUA CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
EAST KINGSTON ULSTER CO	CITY CLINIC BRIGHAM STREET	ALL	✓	✓	✓		
EAST ROCHESTER MONROE CO	V D CLINIC 113 WEST AVE	ALL	✓	✓	✓		
ELMIRA CHEMUNG CO	CITY DISPENSARY 425 EAST MARKET ST	ALL	✓	✓	✓		
ELMONT NASSAU CO	V D CLINIC 765 HEMPSTEAD TURN	ALL	✓	✓	✓		
ENDICOTT BROOME CO	VILLAGE CLINIC 412 EAST MAIN ST	ALL	✓	✓	✓		
FAR ROCKAWAY L I QUEENS CO	CITY CLINIC 1517 CENTRAL AVE	ALL	✓	✓	✓		
FLUSHING L I QUEENS CO	FLUSHING CORONA CLI 3433 JUNCTION BLVD	ALL	✓	✓	✓		
FLUSHING L I QUEENS CO	FLUSHING HOSPITAL PARSONS BLVD	ALL	✓			✓	
FREEPORT NASSAU CO	V D CLINIC MUNICIPAL BLDG	ALL	✓	✓	✓		
FULTON OSWEGO CO	V D CLINIC 192 S FIRST ST	ALL	✓	✓	✓		
GENEVA ONTARIO CO	CITY CLINIC GENEVA GENERAL HOSP	ALL	✓	✓	✓		
GLEN COVE NASSAU CO	V D CLINIC 50 GLEN ST	ALL	✓	✓	✓		
GLENS FALLS WARREN CO	SOCIAL HYG CLINIC 59 RIDGE ST	ALL	✓	✓	✓		

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NEW YORK

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			SYPHILIS	GONORRHEA	FREE	PART-PAY	PAY
GLOVERSVILLE FULTON CO	HEALTH DEPT CLINIC 19 W FULTON ST	ALL	✓	✓	✓		
GOUVERNEUR ST LAWRENCE CO	V D CLINIC 25 JOHN ST	ALL	✓	✓	✓		
GREENBURGH WESTCHESTER CO	COUNTY HEALTH DEPT 25 MCLEAN AVE	ALL	✓		✓		
HORNELL STEUBEN CO	COUNTY HEALTH DEPT 108 BROADWAY	ALL	✓	✓	✓		
HUDSON COLOMBIA CO	SYPHILIS CLINIC 613 WARREN ST	ALL	✓	✓	✓		
HUDSON FALLS WASHINGTON CO	CO SYPHILIS CLINIC 235 MAIN STAIN ST	ALL	✓	✓	✓		
ITHACA TOMPKINS CO	V D CLINIC 115 N TIOGA ST	ALL	✓	✓	✓		
JAMAICA L I QUEENS CO	JAMAICA WEST CLINIC 9218 149TH ST	ALL	✓	✓	✓		
JAMAICA L I QUEENS CO	QUEENS GENERAL HOSP 161ST ST AND 82ND DR	ALL	✓	✓	✓		
JAMESTOWN CHAUTAUQUA CO	SOCIAL HYG CLINIC 4 FOREST AVE	ALL	✓	✓	✓		
JOHNSON CITY BROOME CO	DR FARRELLS OFFICE 301 MAIN ST	ALL	✓	✓		✓	
JOHNSON CITY BROOME CO	ENDICOTT JOHNSON CL 65 BROAD ST	ALL	✓	✓	✓		
JOHNSTOWN FULTON CO	PHYSICIANS OFFICE 9 S WILLIAM ST	ALL	✓	✓	✓		
KENMORE ERIE CO	COUNTY CLINIC 2770 DELAWARE AVE	ALL	✓		✓		
KINGSTON ULSTER CO	BD OF HEALTH CLINIC 27 E OREILLY ST	ALL	✓	✓	✓		
LACKAWANNA ERIE CO	COM MEDICAL CLINIC 195 RIDGE RD	ALL	✓	✓	✓		
LACKAWANNA ERIE CO	LADY OF VICTORY HOSP SO PARK AND RIDGE RD	ALL	✓		✓		
LAWRENCE NASSAU CO	V D CLINIC 105 WASHINGTON AVE	ALL	✓	✓	✓		
LITTLE FALLS HERKIMER CO	V D CLINIC CITY HALL	ALL	✓		✓		
LOCKPORT NIAGARA CO	HEALTH CENTER FIRE HEADQTS BLDG	ALL	✓	✓	✓		
LONG ISLAND QUEENS CO	ST JOHNS HOSP OPD JACKSON AND 12TH ST	ALL	✓	✓	✓	✓	
MALONE FRANKLIN CO	HYDE HOSP CLINIC PARK STREET	ALL	✓	✓	✓		
MAMORONECK WESTCHESTER CO	COUNTY HEALTH DEPT 234 STANLEY AVE	ALL	✓		✓		
MIDDLETOWN ORANGE CO	BD OF HEALTH CLINIC CITY HALL	ALL	✓	✓	✓		
MINEOLA NASSAU CO	V D CLINIC 77 MAIN ST	ALL	✓	✓	✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
MONTICELLO SULLIVAN CO	CITY CLINIC BUSHNELL BLDG	ALL	✓		✓		
MOUNT VERNON WESTCHESTER CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
NEWBURGH ORANGE CO	BD OF HEALTH CLINIC 255 BROADWAY	ALL	✓	✓	✓		
NEW ROCHELLE WESTCHESTER CO	HEALTH DEPT CLINIC 30 CHURCH ST	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	BEEKMAN HOSP CLINIC 117 BEEKMAN ST	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	BELLEVUE HOSP CLINIC 1ST AVE AND 26TH ST	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	BERWIND HOSP OPD 125 E 103RD ST	W	✓	✓	✓		
NEW YORK NEW YORK CO	BETH DAVID HOSP OPD 1720 SECOND AVE	ALL	✓	✓	✓	✓	
NEW YORK NEW YORK CO	BETH ISRAEL HOSPOPD 17 STUYVEHANT PARK E	ALL	✓	✓	✓	✓	
NEW YORK BRONX CO	BRONX HOSPITAL 169TH AND FULTON	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	CENTRAL CLINIC 130 LEONARD ST	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	CEN HARLEM CLINIC 2238 FIFTH AVE	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	CITY HOSP DISP 535 EAST 80TH ST	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	COLUMBUS HOSP CLINIC 226 E 20TH ST	ALL	✓	✓	✓	✓	
NEW YORK NEW YORK CO	COMMUNITY HOSP OPD 8 ST NICHOLAS PLACE	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	EAST HARLEM CLINIC 158 E 115TH ST	ALL	✓	✓	✓		
NEW YORK BRONX CO	FORDHAM HOSPITAL SOUTHERN AND CROTONA	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	FRENCH HOSPITAL OPD 324 W 30TH ST	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	GENITO URINARY CLIN MOUNT SINAI HOSPITAL						
NEW YORK NEW YORK CO	GOOD SAMARITAN DISP 75 ESSEX ST	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	GOUVERNEUR HOSP GOUVERNEUR SLIP	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	HARLEM HOSPITAL 136TH ST AT LENOX AV	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	INWOOD HOUSE OPD 228 W 15 ST	W	✓	✓	✓		
NEW YORK NEW YORK CO	JEWISH MEMORIAL HOSP BROADWAY AT 196TH ST	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	JOINT DISEASES HOSP 45 E 123RD ST	ALL	✓	✓	✓	✓	

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NEW YORK

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
NEW YORK NEW YORK CO	KNICKERBOCKER HOSP 70 CONVENT AVE	ALL	✓			✓	
NEW YORK BRONX CO	LEBANON HOSPITAL WESTCHESTER AVE	ALL	✓	✓	✓	✓	
NEW YORK NEW YORK CO	LENOX HILL HOSPITAL PARK AVE AND 76TH ST	ALL	✓	✓		✓	
NEW YORK BRONX CO	LINCOLN HOSPITAL 141ST AND CONCORD	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	LOWER W SIDE CLINIC 303 NINTH AVE	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	LUTHERAN HOSPITAL 144TH AND CONVENT	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	MANHATTAN EYE EAR 210 EAST 64TH ST	ALL	✓		✓	✓	
NEW YORK NEW YORK CO	MEINHARD CLINIC 130 EAST 101ST ST	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	METROPOLITAN DISP 535 E 80TH ST	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	MIDTOWN HOSPITAL 309 E 49TH ST	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	MISERICORDIA HOSP 531 E 86TH ST	W C	✓	✓	✓		
NEW YORK BRONX CO	MORRISANIA HOSPITAL 168TH AND GERARD	ALL	✓	✓	✓		
NEW YORK BRONX CO	MOTT HAVEN H CENTER 349 E 140TH ST	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	MT SINAI HOSPITAL 100TH AND MADISON	ALL	✓	✓	✓	✓	
NEW YORK NEW YORK CO	NEW YORK DISPENSARY 34 SPRING ST	ALL	✓	✓	✓	✓	
NEW YORK NEW YORK CO	N Y EYE AND EAR HOSP 2ND AVE AND 13TH ST	ALL	✓			✓	
NEW YORK NEW YORK CO	NEW YORK HOSPITAL 525 E 68TH ST	ALL	✓	✓	✓	✓	
NEW YORK NEW YORK CO	NEW YORK INFIRMARY 321 E 15TH ST	W C	✓	✓	✓	✓	
NEW YORK NEW YORK CO	N Y POLYCLINIC HOSP 341 W 50TH ST	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	NEW YORK UNIVERSITY 463 FIRST AVE	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	NORTHEASTERN DISP 222 E 59TH ST	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	NORTHWESTERN DISP 403 W 36TH ST	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	POST GRAD HOSP OPD 301 E 19TH ST	ALL	✓	✓	✓	✓	
NEW YORK NEW YORK CO	ROOSEVELT HOSPITAL 59TH ST AND 9TH AVE	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	RUPT CRIPPLED HOSP 321 E 42ND ST	ALL	✓			✓	

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
NEW YORK NEW YORK CO	ST CLARES HOSPITAL 415 WEST 51ST ST	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	ST LUKES HOSPITAL AMSTERDAM AND 113TH	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	ST VINCENTS HOSPITAL 7TH AVE AND 11TH ST	ALL	✓	✓	✓	✓	
NEW YORK NEW YORK CO	SALVARSAN CLINIC MONTEFIORE HOSPITAL	M W	✓		✓	✓	
NEW YORK NEW YORK CO	STUYVESANT POLY HOSP 137 SECOND AVE	ALL	✓	✓		✓	
NEW YORK NEW YORK CO	SYDENHAM HOSPITAL 565 MANHATTAN AVE	ALL	✓	✓		✓	
NEW YORK BRONX CO	TREMONT CLINIC 1826 ARTHUR AVE	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	VANDERBILT CLINIC BROADWAY AT 167TH ST	ALL	✓			✓	
NEW YORK NEW YORK CO	V D CLINIC 1 EAST 105	ALL	✓			✓	
NEW YORK NEW YORK CO	V D CLINIC HARLEM EYE EAR HOSP	ALL	✓			✓	
NEW YORK NEW YORK CO	WASHINGTON CLINIC 128 PRINCE ST	ALL	✓	✓	✓		
NEW YORK NEW YORK CO	WASH HTS SOC HYG CL 600 WEST 168TH ST	ALL		✓	✓		
NEW YORK NEW YORK CO	WEST SIDE HOSPITAL 446 W 43RD ST	ALL	✓	✓	✓	✓	
NIAGARA FALLS NIAGARA CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
NORTH TONAWANDA NIAGARA CO	V D CLINIC CITY HALL	ALL	✓		✓		
NORWICH CHENANGO CO	CHENANGO MEM HOSP 179 N BROAD ST	ALL	✓		✓		
OGDENSBURG ST LAWRENCE CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
OLEAN CATTARAUGUS CO	CITY CLINIC CITY BUILDING	ALL	✓	✓	✓		
ONEIDA MADISON CO	CITY CLINIC ONEIDA CITY HOSPITAL	ALL	✓	✓	✓		
ONEONTA OSWEGO CO	PHYSICIANS OFFICES	ALL	✓	✓	✓		
OSSINING WESTCHESTER CO	OSSINING HOSPITAL 9PRING STREET	ALL	✓		✓		
OSWEGO OSWEGO CO	V D CLINIC 252 W FIRST	ALL	✓	✓	✓		
PEEKSKILL WESTCHESTER CO	COUNTY HEALTH DEPT MUNICIPAL BLDG	ALL	✓		✓		
PLATTSBURG CLINTON CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
PORT CHESTER WESTCHESTER CO	HEALTH CENTER 350 N MAIN ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
POUGHKEEPSIE DUTCHESS CO	HEALTH SD V O CONTRL 24 WASHINGTON ST	ALL	✓	✓	✓		
POUGHKEEPSIE DUTCHESS CO	COUNTY HEALTH CENTER 14 FAIRMONT AVE	ALL	✓	✓	✓		
ROCHESTER MONROE CO	BADEN ST DISPENSARY 160 BADEN ST	ALL	✓	✓	✓	✓	✓
ROCHESTER MONROE CO	GENESEE HOSPITAL 224 ALEXANDER ST	ALL	✓			✓	
ROCHESTER MONROE CO	HIGHLAND HOSPITAL 3 BELLEVUE DRIVE	ALL	✓		✓	✓	✓
ROCHESTER MONROE CO	ROCHESTER GEN HOSP 501 MAIN ST WEST	ALL	✓	✓	✓		
ROCHESTER MONROE CO	ST MARYS HOSPITAL 909 W MAIN ST	ALL	✓	✓	✓		✓
ROCHESTER MONROE CO	STRONG MEMORIAL HOSP 260 CRITTENDEN BLVD	ALL	✓	✓	✓	✓	✓
ROME ONEIDA CO	SYPH CONT CLINIC 119 E DOMINICK ST	ALL	✓	✓	✓		
SALAMANCA CATTARAUGUS CO	COUNTY CLINIC 27 MAPLE ST	ALL	✓	✓	✓		
SARANAC LAKE FRANKLIN CO	V D CLINIC TOWN HALL MAIN ST	ALL	✓	✓	✓		
SARATOGA SPRINGS SARATOGA CO	CO V D CLINIC SARATOGA HOSPITAL	ALL	✓	✓	✓		
SCHENECTADY SCHENECTADY CO	CO P H COMMITTEE 508 UNION ST	ALL	✓	✓	✓		
SODUS WAYNE CO	OR A O RYANS OFFICE 81 MAIN ST	ALL	✓	✓		✓	
STATEN ISLAND RICHMOND CO	OLD COURT HOUSE CL 302 CENTER AVE	ALL	✓	✓	✓		
STATEN ISLAND RICHMOND CO	RICHMOND V D CLINIC 51 STUYVESANT PLACE	ALL	✓	✓	✓		
STATEN ISLAND RICHMOND CO	ST VINCENTS CLINIC WEST NEW BRIGHTON	F C		✓		✓	
SYRACUSE ONONDAGA CO	SOCIAL HYG CLINIC 610 E FAYETTE ST	ALL	✓	✓		✓	
TARRYTOWN WESTCHESTER CO	TARRYTOWN HOSPITAL WOOD COURT	ALL	✓		✓		
TONAWANDA ERIE CO	CITY CLINIC 201 FLETCHER ST	ALL	✓		✓		
TROY RENNSSELAER CO	MUNICIPAL CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
TROY RENSSELAER CO	TROY HOSPITAL OAKWOOD AVE	ALL	✓	✓	✓		✓
TUPPER LAKE FRANKLIN CO	MERCY GENERAL HOSP 114 WANBEEK AVE	ALL	✓	✓	✓		
UTICA ONEIDA CO	UTICA DISPENSARY 406 ELIZABETH ST	ALL	✓	✓	✓	✓	✓
VALHALLA WESTCHESTER CO	GRASSLANDS HOSPITAL	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC . NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
WARSAW WYOMING CO	CO COMMUNITY HOSP 113 W BUFFALO ST	ALL	✓	✓	✓		
WATERTOWN JEFFERSON CO	V D CLINIC 113 PARK PLACE	ALL	✓	✓	✓		
WATKINS GLEN SCHUYLER CO	COUNTY V D CLINIC FRANKLIN ST	ALL	✓	✓	✓		
WELLSVILLE ALLEGANY CO	CITY CLINIC 233 N MAIN ST	ALL	✓	✓	✓		
WHITEHALL WASHINGTON CO	SYPHILIS CLINIC 1 N MAIN ST	ALL	✓	✓	✓		
WHITE PLAINS WESTCHESTER CO	HEALTH DEPT CLINIC 10 DEPOT PLAZA	ALL	✓		✓		
YONKERS WESTCHESTER CO	SOCIAL HYG CLINIC NEPPERHAN AVE	ALL	✓	✓	✓		
	NORTH CAROLINA						
ACME BLADEN CO	COUNTY V D CLINIC EAST ARCADIA	ALL	✓		✓		
ADOOR MOORE CO	COUNTY HEALTH DEPT CLINIC HOUSE	ALL	✓	✓	✓		
AHOSKIE HERTFORD CO	COUNTY HEALTH DEPT VANN WAREHOUSE BLDG	ALL	✓	✓	✓		
ALBEMARLE STANLY CO	COUNTY HEALTH DEPT LIBRARY BLDG	ALL	✓	✓	✓		
ANDREWS CHEROKEE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
APEX WAKE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
ARDEN BUNCOMBE CO	COUNTY HEALTH DEPT REDMON HALL	ALL	✓	✓	✓		
ASHEBORO RANDOLPH CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
ASHEVILLE BUNCOMBE CO	COUNTY HEALTH DEPT COURTHOUSE JAIL	ALL	✓	✓	✓		
ASHEVILLE BUNCOMBE CO	CITY HEALTH DEPT MARKET BUILDING	ALL	✓	✓	✓		
ATKINSON PENDER CO	V D CLINIC LEWIS BUILDING	ALL	✓	✓	✓		
AVENTON NASH CO	V D CLINIC	ALL	✓	✓	✓		
AYDEN PITT CO	COUNTY HEALTH DEPT TOWN HALL MAIN ST	ALL	✓	✓	✓		
BACHELOR CRAVEN CO	COUNTY MOBILE UNIT ADAMS CREEK	ALL	✓	✓	✓		
BADIN STANLY CO	COUNTY HEALTH DEPT BADIN HOSP BASEMENT	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
BAILEY NASH CO	COUNTY HEALTH DEPT BANK BUILDING	ALL	✓	✓	✓		
BATTLEBORO NASH CO	COUNTY HEALTH DEPT DR A W DEANS OFFICE	ALL	✓	✓	✓		
BEAUFORT CARTARET CO	COUNTY V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
BELHAVEN BEAUFORT CO	COUNTY HEALTH DEPT BANK BUILDING	ALL	✓	✓	✓	✓	
BELMONT GASTON CO	COUNTY HEALTH DEPT DAVIS BUILDING	ALL	✓	✓	✓		
BENSON JOHNSTON CO	COUNTY HEALTH DEPT POST OFFICE	ALL	✓	✓	✓		
BESSEMER CITY GASTON CO	COUNTY HEALTH DEPT OVER CITY HALL	ALL	✓	✓	✓		
BETHEL ANSON CO	ANSON CO MOBILE RURAL AREA	ALL	✓	✓	✓		
BETHEL PITT CO	COUNTY HEALTH DEPT MAIN STREET	ALL	✓	✓	✓		
BEULAVILLE DUPLIN CO	DUPLIN CO MOBILE	ALL	✓	✓	✓		
BLACK MOUNTAIN BUNCOMBE CO	COUNTY HEALTH DEPT HOWERTON BLDG	ALL	✓	✓	✓		
BLADENBORO BLADEN CO	COUNTY V D CLINIC HEALTH DEPT	ALL	✓		✓		
BOONE WATAUGA CO	COUNTY HEALTH DEPT COUNTY OFFICE BLDG	ALL	✓	✓	✓		
BOONVILLE YADKIN CO	COUNTY HEALTH DEPT MAIN STREET	ALL	✓	✓	✓		
BREVARD TRANSYLVANIA CO	HEALTH DEPT CLINIC TINSLEY BLDG	ALL	✓	✓	✓		
BRIDGETON CRAVEN CO	CRAVEN CO MOBILE	ALL	✓	✓	✓		
BRYSON CITY SWAIN CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
BURGAW PENDER CO	V D CLINIC WOLFE BUILDING	ALL	✓	✓	✓		
BURLINGTON ALAMANCE CO	COUNTY HEALTH DEPT FISHER ST	ALL	✓	✓	✓		
BURNSVILLE YANCEY CO	HEALTH DEPT CLINIC BRIGGS BLDG	ALL	✓	✓	✓		
CAIRO ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
CALYPSO DUPLIN CO	DUPLIN CO MOBILE	ALL	✓	✓	✓		
CAMERON MOORE CO	V D CLINIC CARTHAGE STREET	ALL	✓	✓	✓		
CANDLER BUNCOMBE CO	COUNTY HEALTH DEPT DR WILLIS OFFICE	ALL	✓	✓	✓		
CANTON HAYWOOD CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
CARTHAGE MOORE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
CASONS OLD FIELD ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
CEDAR HILLS ANSON CO	ANSON CO MOBILE HIGHWAY 52 NORTH	ALL	✓	✓	✓		
CHADBOURN COLUMBUS CO	COUNTY HEALTH DEPT LEGION HUT	ALL	✓	✓	✓		
CHAPEL HILL ORANGE CO	COUNTY HEALTH DEPT HEALTH DEPT BLDG	ALL	✓	✓	✓		
CHARLOTTE MECKLENBURG CO	CITY HEALTH DEPT 615 E 4TH ST	ALL	✓	✓	✓		
CHARLOTTE MECKLENBURG CO	COUNTY HEALTH DEPT MT HOLLY ROAD RT 6	ALL	✓		✓		
CHARLOTTE MECKLENBURG CO	STEELE CR MAT CLINIC ROUTE NO 3	ALL	✓		✓		
CHEROKEE SWAIN CO	RESERVATION HOSP	ALL	✓	✓	✓		
CHERRYVILLE GASTON CO	COUNTY HEALTH DEPT OVER CITY HALL	ALL	✓	✓	✓		
CHINA GROVE ROWAN CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CHINQUAPIN DUPLIN CO	DUPLIN CO MOBILE	ALL	✓	✓	✓		
CLARKTON BLADEN CO	COUNTY HEALTH DEPT C S CLARK BLDG	ALL	✓		✓		
CLAYTON JOHNSTON CO	V D CLINIC TOWN HALL	ALL	✓	✓	✓		
CLEVELAND ROWAN CO	COUNTY HEALTH DEPT MAIN STREET	ALL	✓	✓	✓		
CLIFFSIDE RUTHERFORD CO	URS MOSS AND JONES DOCTORS OFFICE	ALL	✓	✓	✓		
CLINTON SAMPSON CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
COLERAIN BERTIE CO	COUNTY HEALTH DEPT BANK BLDG 2ND FLOOR	ALL	✓	✓	✓		
COLUMBIA TYRRELL CO	COUNTY HEALTH DEPT AGRICULTURAL BLDG	ALL	✓	✓	✓		
COLUMBUS POLK CO	COUNTY V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
COMO HERTFORD CO	COUNTY HEALTH DEPT TOWN HALL MAIN ST	ALL	✓	✓	✓		
CONCORD CABARRUS CO	COUNTY HEALTH DEPT COUNTY BLDG	ALL	✓	✓	✓		
COOLEEMEE DAVIE CO	COUNTY HEALTH DEPT EPISCOPAL CHURCH	ALL	✓	✓	✓		
COVE CITY CRAVEN CO	CRAVEN CO MOBILE	ALL	✓	✓	✓		
COXE BENNETT ANSON CO	ANSON CO MOBILE HIGHWAY 52 NORTH	ALL	✓	✓	✓		

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NORTH CAROLINA

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
CREEDMOOR GRANVILLE CO	COUNTY HEALTH DEPT OR THOMPSONS OFFICE	ALL	✓	✓	✓		
CRESWELL WASHINGTON CO	COUNTY HEALTH DEPT UR J M PHELPS OFFICE	ALL	✓	✓	✓		
CROSS ROADS CHOWAN CO	COUNTY V D CLINIC WOMANS CLUB BLDG	ALL	✓	✓	✓		
CURRITUCK CURRITUCK CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
DAVIDSON MECKLENBURG CO	COUNTY HEALTH DEPT	ALL	✓		✓		
DEEP CREEK ANSON CO	ANSON CO MOBILE MR G K LITTLES STORE	ALL	✓	✓	✓		
DOBSON SURRY CO	COUNTY HEALTH DEPT COUNTY JAIL	ALL	✓	✓	✓		
DOVER CRAVEN CO	CRAVEN CO MOBILE	ALL	✓	✓	✓		
DUNN HARNETT CO	COUNTY HEALTH DEPT SOUTH WILSON AVE	ALL	✓	✓	✓		
DURHAM DURHAM CO	COUNTY V D CLINIC WHITEROCK BAPTIST CH	ALL	✓	✓	✓		
DURHAM DURHAM CO	HEALTH DEPT CLINIC COURTHOUSE	ALL	✓	✓	✓		
DURHAM DURHAM CO	DUKE HOSPITAL	ALL	✓	✓	✓		✓
DURHAM DURHAM CO	LINCOLN HOSPITAL	N	✓				✓
DURHAM DURHAM CO	WATTS HOSPITAL	ALL	✓	✓			✓
EDENTON CHOWAN CO	CROSS ROADS CLINIC ROUTE 1	ALL	✓	✓	✓		
EDENTON CHOWAN CO	HEALTH DEPT CLINIC BANK OF EDENTON BLDG	ALL	✓	✓	✓		
ELIZABETH CITY PASQUOTANK CO	CITY HEALTH DEPT KRAMER BLDG	ALL	✓	✓	✓		
ELIZABETHTOWN BLADEN CO	COUNTY HEALTH DEPT	ALL	✓		✓		
ELKIN SURRY CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
ELLERBE RICHMOND CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓		✓		
ELM CITY WILSON CO	COUNTY HEALTH DEPT UR PUTNEYS OFFICE	ALL	✓	✓	✓		
ELM GROVE LENOIR CO	COUNTY MOBILE UNIT	ALL	✓		✓		
ENFIELD HALIFAX CO	COUNTY HEALTH DEPT WHITEHEAD DRUGS BLDG	ALL	✓	✓	✓		
ENGLEHARD HYDE O	COUNTY HEALTH DEPT WILLIAMS STORE BLDG	ALL	✓	✓	✓		
FAIRMONT ROBESON CO	COUNTY HEALTH DEPT GRANTHAM BLDG	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
FAISON DUPLIN CO	DUPLIN CO MOBILE	ALL	✓	✓	✓		
FALLING CREEK LENOIR CO	LENOIR CO MOBILE	ALL	✓		✓		
FARMVILLE PITT CO	COUNTY HEALTH DEPT MCKINNEYS HALL	ALL	✓	✓	✓		
FAYETTEVILLE CUMBERLAND CO	COUNTY HEALTH DEPT COURTHOUSE BASEMENT	ALL	✓	✓	✓		
FOREST CITY RUTHERFORD CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
FORT BARNWELL CRAVEN CO	CRAVEN CO MOBILE	ALL	✓	✓	✓		
FRANKLIN MACON CO	HEALTH DEPT CLINIC ASHER BLDG	ALL	✓	✓	✓		
FREMONT WAYNE CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
FUQUAY SPRINGS WAKE CO	COUNTY HEALTH DEPT ELLIOTT BLDG	ALL	✓	✓	✓		
GARLAND SAMPSON CO	COUNTY HEALTH DEPT DR JOHNSONS OFFICE	ALL	✓	✓	✓		
GARRIS GROVE ANSON CO	ANSON CO MOBILE HIGHWAY 109 NORTH	ALL	✓	✓	✓		
GASTON NORTHAMPTON CO	COUNTY HEALTH DEPT POST OFFICE BLDG	ALL	✓		✓		
GASTONIA GASTON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
GATESVILLE GATES CO	COUNTY V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
GOLDSBURO WAYNE CO	COUNTY V D CLINIC COUNTY HOME	ALL	✓	✓	✓		
GOLDSBORO WAYNE CO	COUNTY V D CLINIC COUNTY JAIL	ALL	✓	✓	✓		
GOLDSBORO WAYNE CO	GOLDSBORO HOSPITAL	ALL	✓	✓	✓		
GOLDSBORO WAYNE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
GOWERS LENOIR CO	LENOIR CO MOBILE	ALL	✓		✓		
GRAHAM ALAMANCE CO	COUNTY HEALTH DEPT 3RD FLOOR COURTHOUSE	ALL	✓	✓	✓		
GRAINGERS LENOIR CO	LENOIR CO MOBILE	ALL	✓		✓		
GRANDY CURRITUCK CO	COUNTY HEALTH DEPT WOODHOUSE BLDG	ALL	✓	✓	✓		
GRANITE FALLS CALDWELL CO	COUNTY HEALTH DEPT PARKS BUILDING	ALL	✓	✓	✓		
GREEN HILL ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
GREENSBORO GUILFORD CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		

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NORTH CAROLINA

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			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
GREENVILLE PITT CO	COUNTY HEALTH OEPT 2ND FLOOR CO BLOG	ALL	✓	✓	✓		
HALIFAX HALIFAX CO	COUNTY V O CLINIC HEALTH OEPT	ALL	✓	✓	✓		
HAMLET RICHMONO CO	COUNTY HEALTH OEPT CITY HALL	ALL	✓		✓		
HANES FOHSYTH CO	COUNTY HEALTH OEPT	ALL	✓	✓	✓		
HAHRELLSVILLE HERTFORO CO	COUNTY HEALTH OEPT	ALL	✓	✓	✓		
HAVELOCK CRAVEN CO	COUNTY MOBILE UNIT HYMAN CHURCH	ALL	✓	✓	✓		
HAVELOCK CRAVEN CO	COUNTY MOBILE UNIT WHITLEYS STATION	ALL	✓	✓	✓		
HAVELOCK CRAVEN CO	COUNTY MOBILE UNIT CHERRYPOINT	ALL	✓	✓	✓		
HAYESVILLE CLAY CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
HENOERSON VANCE CO	OR BECKFOROS OFFICE	ALL	✓	✓	✓		
HENOERSON VANCE CO	COUNTY HEALTH OEPT GARNETT ST	ALL	✓	✓	✓		
HICKORY CATAWBA CO	COUNTY HEALTH DEPT CLINES BLOG	ALL	✓	✓	✓		
HIGHPOINT GUILFORO CO	CITY HEALTH OEPT 112 NO WHEEN ST	ALL	✓	✓	✓		
HILLSBORO ORANGE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
HOFFMAN RICHMONO CO	COUNTY HEALTH OEPT DR CAODELLS OFFICE	ALL	✓		✓		
HOOKERTON GREENE CO	COUNTY HEALTH OEPT DRS OFFICE MAIN ST	ALL	✓		✓		
HOPE MILLS CUMBERLANO CO	COUNTY V O CLINIC HEALTH CENTEH	ALL	✓	✓	✓		
HOHNE SCHOOL ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
HOSKINS MECKLENBURG CO	COUNTY V O CLINIC HEALTH OEPT	ALL	✓		✓		
HUGO LENOIR CO	LENOIH CO MOBILE	ALL	✓		✓		
HUNTERSVILLE MECKLENBUHG CO	COUNTY HEALTH OEPT OR T CHAVENS OFFICE	ALL	✓	✓	✓		
INSTITUTE LENOIR CO	LENOIR CO MOBILE	ALL	✓		✓		
JACKSON NORTHAMPTON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
JACKSON NOHTHAMPTON CO	RANSON SCHOOL THE NECK	ALL	✓	✓	✓		
JACKSONVILLE ONSLOW CO	V D CLINIC	ALL	✓	✓	✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
JAMESVILLE MARTIN CO	COUNTY V D CLINIC	ALL	✓	✓	✓		
JEFFERSON ASHE CO	COUNTY HEALTH DEPT ASHE MEMORIAL HOSP	ALL	✓	✓	✓		
KANNAPOLIS CABARRUS CO	COUNTY HEALTH DEPT MAIN STREET	ALL	✓	✓	✓		
KELFORD BERTIE CO	COUNTY V D CLINIC TOWN BLDG	ALL	✓	✓	✓		
KENANSVILLE DUPLIN CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
KENANSVILLE DUPLIN CO	COUNTY MOBILE UNIT SARECTA TRAILER CLNC	ALL	✓	✓	✓		
KENLY JOHNSTON CO	COUNTY HEALTH DEPT DR WOODWARDS OFFICE	ALL	✓	✓	✓		
KERNERSVILLE FORSYTH CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
KERR SAMPSON CO	COUNTY HEALTH DEPT DR COX OFFICE	ALL	✓	✓	✓		
KING STOKES CO	COUNTY HEALTH DEPT MAIN ST	ALL	✓	✓	✓		
KINGS MOUNTAIN CLEVELAND CO	COUNTY HEALTH DEPT CITY HALL BASEMENT	ALL	✓	✓	✓		
KINSTON LENOIR CO	COUNTY HEALTH DEPT SOUTH QUEEN ST	ALL	✓		✓		
KINSTON LENOIR CO	LENOIR CO MOBILE ED JONES STORE	ALL	✓		✓		
KINSTON LENOIR CO	LENOIR CO MOBILE W W JONES STORE	ALL	✓		✓		
KINSTON LENOIR CO	LENOIR CO MOBILE KILPATRICKS STATION	ALL	✓		✓		
KINSTON LENOIR CO	LENOIR CO MOBILE WOOTENS CROSS ROAD	ALL	✓		✓		
KITTRELL VANCE CO	V D CLINIC COLORED SCHOOL	N	✓	✓	✓		
LA GRANGE LENOIR CO	LENOIR CO MOBILE	ALL	✓		✓		
LAURINBURG SCOTLAND CO	COUNTY V D CLINIC COUNTY COURTHOUSE	ALL	✓		✓		
LAWNDALE CLEVELAND CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
LEAKSVILLE ROCKINGHAM CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
LEGGETT EDGECOMB CO	COUNTY V D CLINIC LAWRENCE STORE	ALL	✓	✓	✓		
LENOIR CALDWELL CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
LEXINGTON DAVIDSON CO	COUNTY HEALTH DEPT VARNER BLDG MAIN ST	ALL	✓	✓	✓		
LIBERTY RANDOLPH CO	COUNTY HEALTH DEPT SMITH BLDG	ALL	✓		✓		

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			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
LILLINGTON HARNETT CO	COUNTY HEALTH DEPT AGRICULTURE BLOG	ALL	✓	✓	✓		
LILESVILLE ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
LINCOLNTON LINCOLN CO	COUNTY HEALTH DEPT COUNTY COURTHOUSE	ALL	✓	✓	✓		
LITTLETON HALIFAX CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
LONG PINE ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
LOUISBURG FRANKLIN CO	COUNTY HEALTH DEPT NORTH MAIN ST	ALL	✓	✓	✓		
LUMBERTON ROBESON CO	COUNTY HEALTH DEPT AGRICULTURAL BLDG	ALL	✓	✓	✓		
MCFARLAND ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
MAIDEN CATAWBA	COUNTY V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
MANTEO DARE CO	COUNTY HEALTH DEPT COMMUNITY BLDG	ALL	✓	✓	✓		
MARSHVILLE UNION CO	COUNTY HEALTH DEPT UNION DRUG CO BLDG	ALL	✓	✓	✓		
MATTHEWS MACKLENBURG CO	COUNTY HEALTH DEPT DR T N REIUS OFFICE	ALL	✓		✓		
MAXTON ROBESON CO	COUNTY HEALTH DEPT CARPENTER BLDG	ALL	✓	✓	✓		
MAYODAN ROCKINGHAM CO	COUNTY HEALTH DEPT OVER SHARONS MARKET	ALL	✓	✓	✓		
MEBANE ALAMANCE CO	COUNTY HEALTH DEPT TOWN HALL	ALL	✓	✓	✓		
MIDDLESEX NASH CO	COUNTY HEALTH DEPT DR POWELLS OFFICE	ALL	✓	✓	✓		
MINT HILL MECKLENBURG CO	COUNTY HEALTH DEPT	ALL	✓		✓		
MOCKSVILLE DAVID CO	COUNTY HEALTH DEPT MAIN STREET	ALL	✓	✓	✓		
MONROE UNION CO	COUNTY HEALTH DEPT 210 W FRANKLIN ST	ALL	✓	✓	✓		
MORGANTON BURKE CO	COUNTY HEALTH DEPT PRESNELL BLDG	ALL	✓	✓	✓		
MOVEN ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
MT AIRY SURRY CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
MOUNT HOLLY GASTON CO	COUNTY HEALTH DEPT OVER CITY HALL	ALL	✓	✓	✓		
MT OLIVE WAYNE CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
MOUNT PLEASANT CABARRUS CO	COUNTY HEALTH DEPT MAIN ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
MURFREESBORO HERTFORD CO	COUNTY HEALTH DEPT POST OFFICE BLDG	ALL	✓	✓	✓		
MURPHY CHEROKEE CO	COUNTY HEALTH DEPT PARKER BLDG	ALL	✓	✓	✓		
NASHVILLE NASH CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
NEW BERN CRAVEN CO	COUNTY HEALTH DEPT COURTHOUSE BROAD ST	ALL	✓		✓		
NEW BERN CRAVEN CO	GOOD SHEPHERD HOSP WEST STREET	ALL	✓		✓		
NEW BERN CRAVEN CO	CRAVEN CO MOBILE PINE GROVE CHURCH	ALL	✓	✓	✓		
NEWLAND AVERY CO	CITY HEALTH DEPT	ALL	✓	✓	✓		
NEWTON CATAWBA CO	COUNTY HEALTH DEPT COUNTY OFFICE BLDG	ALL	✓	✓	✓		
NORTH HARLOWE CRAVEN CO	CRAVEN CO MOBILE CARTERS BEER GARDEN	ALL	✓	✓	✓		
NORTH HARLOWE CRAVEN CO	CRAVEN CO MOBILE GODETTES STATION	ALL	✓	✓	✓		
NORTH WADESBORO ANSON CO	ANSON CO MOBILE HOUGH SCHOOL HWY 109	ALL	✓	✓	✓		
NORWOOD STANLY CO	COUNTY HEALTH DEPT BARRINGER BLDG	ALL	✓		✓		
OAK CITY MARTIN CO	COUNTY V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
OXFORD GRANVILLE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
PEE DEE ANSON CO	ANSON CO MOBILE ROBINSONS STORE	ALL	✓	✓	✓		
PEMBROKE ROBESON CO	COUNTY HEALTH DEPT RAILROAD STREET	ALL	✓	✓	✓		
PENDLETON NORTHAMPTON	COUNTY V D CLINIC	ALL	✓	✓	✓		
PILOT MOUNTAIN SURRY CO	COUNTY HEALTH DEPT MAIN STREET	ALL	✓	✓	✓		
PINEHURST MOORE CO	COUNTY HEALTH DEPT FIRE HOUSE	ALL	✓	✓	✓		
PINETOPS EDGECOMBE CO	EDGECOMBE CO MOBILE STORE BLDG	ALL	✓	✓	✓		
PINEVILLE MECKLENBERG CO	COUNTY HEALTH DEPT	ALL	✓		✓		
PINEY WOOD SCHOOL ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
PINK HILL LENOIR CO	LENOIR CO MOBILE	ALL	✓		✓		
PITTSBORO CHATHAM CO	COUNTY HEALTH DEPT HEALTH DEPT BLDG	ALL	✓	✓	✓		
PLYMOUTH WASHINGTON CO	COUNTY HEALTH DEPT WASHINGTON CO HOME	ALL	✓	✓	✓		

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NORTH CAROLINA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
POLKTON ANSON CO	ANSON CO MOBILE RAILROAD STATION	ALL	✓	✓	✓		
POPLAR HILL CH ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
RALEIGH WAKE CO	NEW REX HOSPITAL	ALL	✓	✓		✓	
RALEIGH WAKE CO	COUNTY HEALTH DEPT OLD REX HOSP BLDG	ALL	✓	✓	✓		
RAMSEUR RANDOLPH CO	COUNTY HEALTH DEPT COLERIDGE BANK BLDG	ALL	✓	✓	✓		
RED HILL SCHOOL ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
RED SPRINGS ROBESON CO	COUNTY HEALTH DEPT BANK BLDG MAIN ST	ALL	✓	✓	✓		
REIDSVILLE ROCKINGHAM CO	COUNTY HEALTH DEPT COMMUNITY BLDG	ALL	✓	✓	✓		
RHEMS LENOIR CO	LENOIR CO MOBILE SIMMONS STATION	ALL	✓	✓	✓		
RICHLANDS ONSLOW CO	V U CLINIC	ALL	✓	✓	✓		
RICH SQUARE NORTHAMPTON CO	COUNTY HEALTH DEPT MATTRESS FACTORY BLD	ALL	✓	✓	✓		
ROANOKE RAPIDS HALIFAX CO	COUNTY HEALTH DEPT ROSEMARY CLINIC BLDG	ALL	✓	✓	✓		
ROBBINSVILLE GRAHAM CO	COUNTY HEALTH DEPT INGRAMS BLDG	ALL	✓	✓	✓		
ROBERSONVILLE MARTIN CO	COUNTY HEALTH DEPT MAIN ST	ALL	✓	✓	✓		
ROCKINGHAM RICHMOND CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓		✓		
ROCKY FORD CH ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
ROCKY MOUNT EDGECOMBE CO	CITY HEALTH DEPT MUNICIPAL BLDG	ALL	✓	✓	✓		
ROSEBORO SAMPSON CO	COUNTY HEALTH DEPT HARRIS BLDG	ALL	✓	✓	✓		
ROSEHILL DUPLIN CO	DUPLIN CO MOBILE	ALL	✓	✓	✓		
ROWLAND ROBESON CO	COUNTY HEALTH DEPT MAIN STREET	ALL	✓	✓	✓		
ROXBORO PERSON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
RURAL HALL FORSYTH CO	COUNTY HEALTH DEPT DR FLYNTS FORMER OFC	ALL	✓	✓	✓		
RUTHERFORD COLLEG BURKE CO	COUNTY HEALTH DEPT VALDESE COLLEGE HOSP	ALL	✓	✓	✓		
RUTHERFORDTON RUTHERFORD CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
ST PAULS ROBESON CO	COUNTY HEALTH DEPT BANK BLDG BROAD ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
SALISBURY ROWAN CO	COUNTY HEALTH OEPT COURTHOUSE	ALL	✓	✓	✓		
SALISBURY ROWAN CO	COUNTY V U CLINIC COUNTY HOME	ALL	✓	✓	✓		
SANFORO LEE CO	LEE CO HOSPITAL	ALL	✓		✓		
SAXAPAHAW ALAMANCE CO	V U CLINIC SELLARS MFG CO OFC	ALL	✓	✓	✓		
SCOTLANO NECK HALIFAX CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SEABOARO NORTHAMPTON CO	COUNTY HEALTH UEPT	ALL	✓	✓	✓		
SHARPSBURG NASH CO	V U CLINIC	ALL	✓	✓	✓		
SHELBY CLEVELANO CO	COUNTY HEALTH OEPT WETHERS BLANTON BLUG	ALL	✓	✓	✓		
SILER CITY CHATHAM CO	COUNTY HEALTH OEPT MUNICIPAL BLOG	ALL	✓	✓	✓		
SMITHFIELO JOHNSTON CO	COUNTY HEALTH UEPT COURTHOUSE	ALL	✓	✓	✓		
SMITHFIELO JOHNSTON CO	COUNTY HEALTH OEPT UPPURTUNITY HALL	ALL	✓	✓	✓		
SNOW HILL GREENE CO	COUNTY HEALTH OEPT AGRICULTURAL BLOG	ALL	✓		✓		
SOUTHPORT BRUNSWICK CO	COUNTY V O CLINIC J A DOSHER MEM HOSP	ALL	✓		✓		
SPARTA ALLEGHANY CO	COUNTY HEALTH OEPT COUNTY COURTHOUSE	ALL	✓	✓	✓		
SPEEO EOGECOMBE CO	EOGECOMBE CO MOBILE RAILROAU STATION	ALL	✓	✓	✓		
SPRING HOPE NASH CO	COUNTY HEALTH DEPT MAYORS OFFICE	ALL	✓	✓	✓		
STANLEY GASTON CO	COUNTY HEALTH DEPT FORMER OFC DR TAYLOR	ALL	✓	✓	✓		
STANTONSBURG WILSON CO	COUNTY HEALTH DEPT DR O B DARDENS OFC	ALL	✓	✓	✓		
STATESVILLE IREDELL CO	COUNTY HEALTH DEPT STEARNS BLDG	ALL	✓	✓	✓		
STEDMAN CUMBERLAND CO	COUNTY V O CLINIC OVER CARTERS STORE	ALL	✓	✓	✓		
STOVALL GRANVILLE CO	COUNTY HEALTH DEPT DR BRADSHERS OFFICE	ALL	✓	✓	✓		
SUNBURY GATES CO	COUNTY V O CLINIC HEALTH DEPT	ALL	✓	✓	✓		
SWANQUARTER HYDE CO	COUNTY HEALTH DEPT AGRICULTURAL BLDG	ALL	✓	✓	✓		
SYLVA JACKSON CO	COUNTY HEALTH DEPT CO COURTHOUSE	ALL	✓	✓	✓		
TABOR CITY COLUMBUS CO	V O CLINIC	ALL	✓		✓		

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NORTH CAROLINA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
TARBORO EDGECOMBE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
THOMASVILLE DAVIDSON CO	COUNTY HEALTH DEPT CITY MUNICIPAL BLDG	ALL	✓	✓	✓		
TRAPHILL WILKES CO	COUNTY HEALTH DEPT MASONIC BLDG	ALL	✓		✓		
TROY MONTGOMERY CO	COUNTY HEALTH DEPT BANK BLDG MAIN ST	ALL	✓		✓		
TRYON POLK CO	ST LUKES HOSPITAL	ALL	✓	✓	✓		
VANCEBORO CRAVEN CO	CRAVEN CO MOBILE	ALL	✓	✓	✓		
WADESBORO ANSON CO	COUNTY HEALTH DEPT AGRICULTURAL BLDG	ALL	✓	✓	✓		
WADESBORO ANSON CO	COUNTY MOBILE UNIT LITTLES FARM HWY 109	ALL	✓	✓	✓		
WAKE FOREST WAKE CO	COUNTY HEALTH DEPT WILKINSON BLDG	ALL	✓	✓	✓		
WALLACE DUPLIN CO	DUPLIN CO MOBILE R F D	ALL	✓	✓	✓		
WALNUT COVE STOKES CO	COUNTY HEALTH DEPT MAIN ST	ALL	✓	✓	✓		
WALSTONBURG GREENE CO	COUNTY HEALTH DEPT DR MARLOWES OFC	ALL	✓		✓		
WARSAW DUPLIN CO	DUPLIN CO MOBILE	ALL	✓	✓	✓		
WASHINGTON BEAUFORT CO	COUNTY HEALTH DEPT AGRICULTURAL BLDG	ALL	✓	✓	✓		
WAXHAW UNION CO	COUNTY HEALTH DEPT GAMBLE DRUG CO BLDG	ALL	✓	✓	✓		
WAYNESVILLE HAYWOOD CO	COUNTY HEALTH DEPT COURTHOUSE MAIN ST	ALL	✓	✓	✓		
WEAVERVILLE BUNCOMBE CO	COUNTY HEALTH DEPT DR SPRINKLES OFFICE	ALL	✓	✓	✓		
WELDON HALIFAX CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
WENDELL WAKE CO	COUNTY HEALTH DEPT UNDERHILL BLDG	ALL	✓	✓	✓		
W SOUTHERN PINES MOORE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
WHITAKERS EDGECOMBE CO	COUNTY HEALTH DEPT DOCTORS OFFICE	ALL	✓	✓	✓		
WHITAKERS EDGECOMBE CO	COUNTY V D CLINIC ETHERIDGE STORE RFD1	ALL	✓	✓	✓		
WHITE STORE ANSON CO	ANSON CO MOBILE	ALL	✓	✓	✓		
WHITEVILLE COLUMBUS CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓		✓		
WILKESBORO WILKES CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓		✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
WILLIAMSTON MARTIN CO	COUNTY HEALTH DEPT CITY HALL MAIN ST	ALL	✓	✓	✓		
WILMINGTON NEW HANOVER CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
WILSON WILSON CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
WINDSOR BERTIE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
WINSTON SALEM FORSYTHE CO	CITY V D CLINIC WAUGHTOWN STREET	ALL	✓	✓	✓		
WINSTON SALEM FORSYTH CO	COUNTY HEALTH DEPT 507 NORTH WEST BLVD	ALL	✓	✓	✓		
WINSTON SALEM FORSYTH CO	HEALTH CENTER 7TH AND HIGHLAND STS	ALL	✓	✓	✓		
WINSTON SALEM FORSYTH CO	OGBURNTOWN H CENTER STYERS BLDG ROUTE 3	ALL	✓	✓	✓		
WINTON HERTFORO CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
YAOKINVILLE YAOKIN CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
ZEBULON WAKE CO	COUNTY HEALTH DEPT PRIVETT BLDG	ALL	✓	✓	✓		
	NORTH DAKOTA **						
GRAND FORKS GRAND FORKS CO	CO WELFARE BD CLINIC 213 S 3RD ST	ALL	✓	✓	✓		
	OHIO						
AOOYSTON HAMILTON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
AKRON SUMMIT CO	CITY HOSPITAL 525 EAST MARKET ST	A	✓	✓	✓		
AKRON SUMMIT CO	CHILDRENS HOSPITAL 182 WEST BOWERY ST	C	✓	✓	✓		
AKRON SUMMIT CO	MUNICIPAL CLINIC 11 EAST EXCHANGE ST	A	✓	✓	✓	✓	
ALLIANCE STARK CO	CITY CLINIC BASEMENT CITY BLDG	ALL	✓	✓		✓	
BELLAIRE BELMONT CO	V D CLINIC OANKWORTH BLDG	ALL	✓	✓	✓	✓	
BELLEFONTAINE LOGAN CO	COUNTY HEALTH BOARO LAWRENCE BLDG	ALL	✓		✓		

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** IN ADDITION TO CLINICS LISTED, THE ADDRESSES OF PHYSICIANS GIVING TREATMENT FOR VENEREAL DISEASES UNDER THE STATE PLAN MAY BE OBTAINED FROM STATE, COUNTY, AND MUNICIPAL OFFICERS.

OHIO

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
CANTON STARK CO	CITY CLINIC AUDITORIUM BLOG	ALL	✓	✓	✓	✓	
CHILLICOTHE ROSS CO	BD OF HEALTH CLINIC 65 EAST 2NO ST	ALL	✓	✓		✓	
CHILLICOTHE ROSS CO	PUBLIC CLINIC 65 EAST MAIN ST	ALL	✓	✓			✓
CINCINNATI HAMILTON CO	BABIES FUND CLINIC 1029 FINULAY ST	C	✓		✓		
CINCINNATI HAMILTON CO	BABIES FUND CLINIC 1041 CUTTER ST	C	✓		✓		
CINCINNATI HAMILTON CO	BABIES FUND CLINIC 320 WOODWARD ST	C	✓		✓		
CINCINNATI HAMILTON CO	BECKMAN DISPENSARY 3212 BURNET AVENUE	W	✓	✓	✓	✓	
CINCINNATI HAMILTON CO	CHILDRENS HOSPITAL ELLAND AND BETHESDA	C	✓		✓		
CINCINNATI HAMILTON CO	GEN HOSP PED O P D BURNET AVE	C	✓	✓	✓	✓	
CINCINNATI HAMILTON CO	CITY WORKHOUSE 3208 COLORIAN AVE	ALL	✓	✓	✓		
CINCINNATI HAMILTON CO	GENERAL HOSPITAL BURNET AND GOODMAN	ALL	✓	✓	✓	✓	
CINCINNATI HAMILTON CO	COUNTY HEALTH DEPT ST SIMON WOODLAWN	ALL	✓	✓	✓		
CINCINNATI HAMILTON CO	COUNTY HEALTH DEPT STEELE SUBDIVISION	ALL	✓	✓	✓		
CINCINNATI HAMILTON CO	CO HOME AND HOSP HARTWELL	A	✓		✓		
CINCINNATI HAMILTON CO	CO T B HOSPITAL GUERLEY ROAD	ALL	✓		✓		
CINCINNATI HAMILTON CO	HEALTH CENTER 212 WEST 12TH ST	ALL	✓	✓	✓		
CINCINNATI HAMILTON CO	HEALTH DEPT CLINIC 503 EAST 3RD ST	A	✓	✓	✓		
CINCINNATI HAMILTON CO	MT ST MARYS TR SCH WARSAW AND GRAND AVE	WC	✓	✓	✓		
CINCINNATI HAMILTON CO	SHOEMAKER CLINIC 1041 CUTTER ST	ALL	✓	✓		✓	
CINCINNATI HAMILTON CO	UNION BETHEL CLINIC 501 EAST THIRD ST	ALL	✓	✓		✓	
CLEVELAND CUYAHOGA CO	CITY HOSP IN PT DEPT 3395 SCRANTON RD	ALL	✓	✓	✓	✓	✓
CLEVELAND CAYAHOGA CO	CITY HOSP OUT PT DEP 3395 SCRANTON RD	ALL	✓	✓	✓	✓	
CLEVELAND CUYAHOGA CO	DIAGNOSTIC CLINIC ROOM 22 CITY HALL	ALL	✓	✓	✓		
CLEVELAND CUYAHOGA CO	CITY HOSP DISP 2500 EAST 35TH ST	C	✓	✓	✓	✓	
CLEVELAND CUYAHOGA CO	FAIRVIEW PARK HOSP 3305 FRANKLIN BLVD	ALL	✓	✓	✓	✓	

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
CLEVELAND CUYAHOGA CO	MT SINAI HOSPITAL 1800 EAST 105TH ST	F		✓	✓	✓	
CLEVELAND CUYAHOGA CO	ST ALEXIS HOSP DISP BROADWAY AND MCBRIDE	ALL	✓		✓	✓	
CLEVELAND CUYAHOGA CO	ST LUKES HOSPITAL 11311 SHAKER BLVD	ALL	✓	✓	✓	✓	
CLEVELAND CUYAHOGA CO	ST VINCENTS HOSP E 22ND ST AT CENTRAL	ALL	✓	✓	✓	✓	✓
CLEVELAND CUYAHOGA CO	U HOSP CHILD CLINIC ADELBERT RD	C	✓		✓	✓	
CLEVELAND CUYAHOGA CO	U HOSP OUT PT DEPT 2065 ADELBERT RD	ALL	✓	✓	✓	✓	✓
COLUMBUS FRANKLIN CO	CHILDRENS HOSPITAL 17TH AND STONE ST	C	✓	✓	✓	✓	
COLUMBUS FRANKLIN CO	PUBLIC HEALTH CLINIC 980 MT VERNON AVE	ALL	✓	✓	✓		
COLUMBUS FRANKLIN CO	STATE INST FOR BLIND	C	✓	✓	✓		
COLUMBUS FRANKLIN CO	BUREAU OF CHARITIES 451 OAK ST	C	✓	✓	✓		
COLUMBUS FRANKLIN CO	UNIVERSITY HOSPITAL OHIO STATE UNIV	A	✓	✓		✓	
COLUMBUS FRANKLIN CO	WHITE CROSS CLINIC WHITE CROSS HOSPITAL	A	✓			✓	
DAYTON MONTGOMERY CO	PUBLIC HEALTH CLINIC 334 NORWOOD AVE	ALL	✓	✓	✓	✓	✓
EAST AKRON SUMMIT CO	COMMUNITY HOSP 15 BROAD ST	ALL	✓	✓			✓
EAST CLEVELAND CUYAHOGA CO	HURON RD HOSPITAL 13951 TERRACE RD	ALL	✓	✓	✓	✓	
EAST LIVERPOOL COLUMBIANA CO	CITY HEALTH CLINIC CITY HALL W 6TH ST	ALL	✓	✓	✓		
HAMILTON BUTLER CO	MERCY HOSP V D CLIN	ALL	✓	✓	✓		
IRONTON LAWRENCE CO	V D CLINIC CITY BLDG	ALL	✓	✓	✓		
LAKEWOOD CUYAHOGA CO	DIVISION OF HEALTH 14517 DETROIT AVE	ALL	✓	✓	✓	✓	✓
LANCASTER FAIRFIELD CO	COUNTY CLINIC COURTHOUSE	A	✓		✓		
LIMA ALLEN CO	MEM HOSP V D CLINIC LINDEN AND MOBILE	ALL	✓	✓	✓		
LOGAN HOCKING CO	COUNTY CLINIC	ALL	✓		✓		
MCARTHUR VINTON CO	COUNTY CLINIC	ALL	✓		✓		
MANSFIELD RICHLAND CO	V D CLINIC CITY BLDG	ALL	✓		✓		
MARION MARION CO	CITY CLINIC DELAWARE AVE	ALL	✓	✓	✓		

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OHIO – OKLAHOMA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY	PAY
MIDDLETOWN BUTLER CO	V D CLINIC 101 NORTH BROAD ST	ALL	✓		✓		
NORWALK HURON CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
OXFORD BUTLER CO	OXFORD COMMUNITY MUNICIPAL BLDG	ALL	✓	✓	✓		
POMEROY MEIGS CO	COUNTY HEALTH DEPT 116 EAST MAIN ST	ALL	✓	✓	✓		
PORT CLINTON OTTAWA CO	THE POOL HOSPITAL 125 EAST THIRD ST	ALL	✓	✓		✓	
PORTSMOUTH SCIOTO CO	HEALTH CENTER CLINIC 501 COURT ST	ALL	✓		✓		
ST CLAIRSVILLE BELMONT CO	COUNTY CLINIC	ALL	✓	✓	✓		
SANDUSKY ERIE CO	V D CLINIC CITY BLDG	ALL	✓	✓	✓		
SIDNEY SHELBY CO	HEALTH DEPT CLINIC COURTHOUSE	ALL	✓	✓	✓		
SPRINGFIELD CLARK CO	MUNICIPAL HOSPITAL EAST HIGH ST	ALL	✓	✓	✓		
TOLEDO LUCAS CO	PUBLIC HEALTH CLINIC 9 ONTARIO ST	ALL	✓	✓	✓		
TOLEDO LUCAS CO	ST VINCENTS DISP 2213 CHERRY ST	ALL	✓		✓		
TROY MIAMI CO	HEALTH DEPT CLINIC 119 WEST MAIN ST	ALL	✓	✓	✓		
WARREN TRUMBULL CO	PUBLIC HEALTH CLINIC 238 NO PARK AVE	ALL	✓	✓	✓		
WARREN TRUMBULL CO	COUNTY CLINIC 303 MAHONING AVE	ALL	✓	✓	✓		
WAVERLY PIKE CO	CO BOARD OF HEALTH	ALL	✓		✓		
ZENIA GREENE CO	COUNTY HEALTH DEPT CITY BLDG	ALL	✓	✓	✓		
YOUNGSTOWN MAHONING CO	V D CLINIC EAST INDIANOLA AVE	ALL	✓	✓	✓	✓	
ZANESVILLE MUSKINGUM CO	CITY CLINIC MARKET HOUSE	ALL	✓	✓	✓	✓	
	OKLAHOMA						
ADA PONTOTOC CO	COUNTY HEALTH DEPT 103 WEST MAIN	ALL	✓	✓	✓		
ANADARKO CADDO CO	COUNTY HEALTH DEPT 325 WEST BROADWAY	ALL	✓	✓	✓		
ANTLERS PUSHMATAHA CO	CO HEALTH DEPT WOODRUFF JONES BLDG	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
ARDMORE CARTER CO	COUNTY HEALTH DEPT FAIRGROUNDS	ALL	✓	✓	✓		
ARNETT ELLIS CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
ATOKA ATOKA CO	COUNTY HEALTH DEPT 207 WEST COURT ST	ALL	✓	✓	✓		
BEAVER BEAVER CO	COUNTY HEALTH DEPT COURTHOUSE BASEMENT	ALL	✓	✓	✓		
BEGGS OKMULGEE CO	CO HEALTH DEPT W P A SEWING ROOM	ALL	✓	✓	✓		
BLANCHARD MCCLAIN CO	COUNTY HEALTH DEPT METHODIST CHURCH	ALL	✓	✓	✓		
BOISE CITY CIMARRON CO	COUNTY HEALTH DEPT COURTHOUSE 2ND FLOOR	ALL	✓	✓	✓		
BOYNTON MUSKOGEE CO	COUNTY HEALTH DEPT BOYNTON HOTEL	ALL	✓	✓	✓		
BRISTOW CREEK CO	COUNTY HEALTH DEPT FREELAND BLDG	ALL	✓	✓	✓		
BROKEN BOW MCCURTAIN CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
BUFFALO HARPER CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
CARNEGIE CADDO CO	COUNTY HEALTH DEPT 14 SO BROADWAY	ALL	✓	✓	✓		
CHEYENNE ROGER MILLS CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CLAREMORE ROGERS CO	V D CLINIC COURTHOUSE BASEMENT	ALL	✓	✓	✓		
COLBERT BRYAN CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
CRESCENT LOGAN CO	COUNTY HEALTH DEPT GODUS DRUG STORE	ALL	✓	✓	✓		
CUSHING PAYNE CO	COUNTY HEALTH DEPT 105 EAST MOSES ST	ALL	✓	✓	✓		
DRUMRIGHT CREEK CO	COUNTY HEALTH DEPT 100 EAST BROADWAY	ALL	✓	✓	✓		
DUNCAN STEPHENS CO	COUNTY HEALTH DEPT ARMORY BLDG	ALL	✓	✓	✓		
DURANT BRYAN CO	COUNTY HEALTH DEPT BROWN BLDG	ALL	✓	✓	✓		
ENID GARFIELD CO	V D CLINIC CONVENTION HALL	ALL	✓	✓	✓		
GUTHRIE LOGAN CO	COUNTY HEALTH DEPT 110 WEST OKLAHOMA AV	ALL	✓	✓	✓		
GUYMON TEXAS CO	COUNTY HEALTH DEPT 105 WEST 5TH ST	ALL	✓	✓	✓		
HEALDTON CARTER CO	COUNTY HEALTH DEPT ARMORY	ALL	✓	✓	✓		
HENNESSEY KINGFISHER CO	COUNTY HEALTH DEPT MEMORIAL HALL	ALL	✓	✓	✓		

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OKLAHOMA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TD *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
HENRYETTA OKMULGEE CO	COUNTY HEALTH DEPT CITY HALL 116 SD 5	ALL	✓	✓	✓		
HUGO CHOCTAW CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
IDABEL MCCURTAIN CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
JAY DELAWARE CO	COUNTY HEALTH DEPT PUBLIC HEALTH BLDG	ALL	✓	✓	✓		
KINGFISHER KINGFISHER CO	COUNTY HEALTH DEPT 119 SOUTH MAIN ST	ALL	✓	✓	✓		
KONAWA SEMINOLE CO	COUNTY HEALTH DEPT HIGHWAY BLDG	ALL	✓	✓	✓		
LANGSTON LOGAN CO	COUNTY HEALTH DEPT UNIVERSITY INFIRMARY	ALL	✓	✓	✓		
LAWTON COMANCHE CO	COUNTY HEALTH DEPT 422 D AVE	ALL	✓	✓	✓		
MCALESTER PITTSBURG CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
MADILL MARSHALL CO	COUNTY HEALTH DEPT W P A BLDG	ALL	✓	✓	✓		
MARIETTA LOVE CO	COUNTY HEALTH DEPT KELLY DRUG STORE	ALL	✓	✓	✓		
MUSKOGEE MUSKOGEE CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
NORMAN CLEVELAND CO	COUNTY HEALTH DEPT 101 EAST EUFAULA	ALL	✓	✓	✓		
NOWATA NOWATA CO	V D CLINIC COMMERCE BANK BLDG	ALL	✓	✓	✓		
OKLAHOMA CITY OKLAHOMA CO	CITY HEALTH DEPT 9 WALL ST	ALL	✓	✓	✓		
OKMULGEE OKMULGEE CO	COUNTY HEALTH DEPT COLORED HOSPITAL	N	✓	✓	✓		
OKMULGEE OKMULGEE CO	CO HEALTH DEPT 718 NO SEMINOLE	W	✓	✓	✓		
OKTAHA MUSKOGEE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
PAULS VALLEY GARVIN CO	COUNTY HEALTH DEPT OVER WORLEYS CAFE	ALL	✓	✓	✓		
PICHER OTTAWA CO	V D CLINIC 801 CONNELL	ALL	✓	✓	✓		
PORTER WAGONER CO	V D CLINIC COUNTY BLDG	ALL	✓	✓	✓		
POTEAU LEFLORE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
PRYOR MAYES CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓	✓	✓		
PURCELL MCCLAIN CO	COUNTY HEALTH DEPT COMMUNITY HALL	ALL	✓	✓	✓		
SALLISAW SEQUOYAH CO	COUNTY HEALTH DEPT OVER STATE BANK	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
SAPULPA CREEK CO	COUNTY HEALTH DEPT PARK AND DEWEY STS	ALL	✓	✓	✓		
SEMINOLE SEMINOLE CO	COUNTY HEALTH DEPT MARKET SQUARE BLDG	ALL	✓	✓	✓		
SHAWNEE POTTAWATOMIE CO	COUNTY HEALTH DEPT 15 WEST 10TH ST	ALL	✓	✓	✓		
STELLA CLEVELAND CO	COUNTY HEALTH DEPT UNION SCHOOL	N	✓	✓	✓		
STILLWATER PAYNE CO	COUNTY HEALTH DEPT 423 MAIN ST	ALL	✓	✓	✓		
STILWELL ADAIR CO	COUNTY HEALTH DEPT OVER EAGLE THEATER	ALL	✓	✓	✓		
TAHLEQUAH CHEROKEE CO	COUNTY HEALTH DEPT 302 SO COLLEGE	ALL	✓	✓	✓		
TISHOMINGO JOHNSTON CO	COUNTY HEALTH DEPT W P A OFFICE	ALL	✓	✓	✓		
TULSA TULSA CO	CITY HEALTH DEPT 21 NO CINCINNATI ST	ALL	✓	✓	✓		
WAGONER WAGONER CO	V D CLINIC MERCANTILE BLDG	ALL	✓	✓	✓		
WATONGA BLAINE CO	COUNTY HEALTH DEPT ARMORY	ALL	✓	✓	✓		
WAURIKA JEFFERSON CO	CO HEALTH DEPT HUNTER BLDG	ALL	✓	✓	✓		
WEWOKA SEMINOLE CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
WOODWARD WOODWARD CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
	OREGON						
ALBANY LINN CO	COUNTY H D CLINIC COUNTY COURTHOUSE	ALL	✓	✓	✓		
ASTORIA CLAPSOP CO	COUNTY HEALTH DEPT FLAVEL MEM HOUSE	ALL	✓	✓	✓		
BAKER BAKER CO	COUNTY HEALTH DEPT COUNTY COURTHOUSE	ALL	✓	✓	✓		
COQUILLE COOS CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓	✓	
EUGENE LANE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
GRAND RONDE POLK CO	V D CLINIC INDIAN SERVICE	ALL	✓		✓		
GRANTS PASS JOSEPHINE CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
HILLSBORO WASHINGTON CO	COUNTY HEALTH DEPT COUNTY COURTHOUSE	ALL	✓	✓	✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
KLAMATH AGENCY KLAMATH CO	COUNTY HEALTH DEPT INDIAN RESERVATION	ALL	✓	✓	✓		
KLAMATH FALLS KLAMATH CO	COUNTY HEALTH DEPT 8TH AND PINE STS	ALL	✓	✓	✓		
LA GRANDE UNION CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
MCMINNVILLE YAMHILL CO	CO HEALTH CLINIC COUNTY COURTHOUSE	ALL	✓	✓	✓		
MARSHFIELD COOS CO	COUNTY HEALTH DEPT HALL BLDG	ALL	✓	✓	✓	✓	
MEDFORD JACKSON CO	COUNTY HEALTH DEPT COUNTY COURTHOUSE	ALL	✓	✓	✓		
OREGON CITY CLACKAMAS CO	COUNTY HEALTH DEPT 304 COURTHOUSE	ALL	✓	✓	✓	✓	
PENDLETON UMATILLA CO	COUNTY HEALTH UNIT CITY HALL	ALL	✓	✓	✓		
PORTLAND MULTNOMAH CO	OREGON UNIV MED SCH 3181 SW MARQUAM HILL	ALL	✓	✓	✓	✓	✓
PORTLAND MULTNOMAH CO	PUBLIC HEALTH CLINIC 231 S W THIRD AVE	ALL	✓	✓	✓		
ROSEBURG DOUGLAS CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
SALEM MARION CO	COUNTY HEALTH DEPT 495 STATE ST	ALL	✓	✓		✓	
SILETZ LINCOLN CO	V D CLINIC INDIAN SERVICE	ALL	✓		✓		
THE DALLES WASCO CO	COUNTY HEALTH UNIT 510 COURT ST	ALL	✓	✓	✓		
	PENNSYLVANIA						
ABINGTON MONTGOMERY CO	ABINGTON MEM HOSP	ALL	✓	✓	✓	✓	✓
ALLENTOWN LEHIGH CO	HOSPITAL LUETIC CL	ALL	✓		✓		
ALLENTOWN LEHIGH CO	SACRED HEART HOSP CHEW ST	ALL	✓	✓	✓	✓	
ALTOONA BLAIR CO	V D CLINIC HINMAN BUILDING	ALL	✓	✓	✓		
ASHLAND SCHUYLKILL CO	ASHLAND STATE HOSP	ALL	✓	✓	✓	✓	
BEAVER FALLS BEAVER CO	PROVIDENCE HOSPITAL 3RD AVE	ALL	✓	✓	✓		
BEDFORD BEDFORD CO	PA DEPT OF HEALTH BRODE BLDG	ALL	✓	✓	✓		
BELLEFONTE CENTRE CO	V D CLINIC WHITE BLDG	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
BETHLEHEM LEHIGH CO	ST LUKES HOSPITAL	ALL	✓	✓	✓	✓	✓
BLAIRSVILLE INDIANA CO	CITY CLINIC 195 NORTH WALNUT ST	ALL	✓	✓	✓		
BLOOMSBURG COLUMBIA CO	BLOOMSBURG HOSPITAL	ALL	✓	✓	✓		
BLOSSBURG TIOGA CO	BLOSSBURG STATE HOSP	ALL	✓	✓	✓		✓
BRADFORD MCKEAN CO	BRADFORD HOSPITAL	ALL	✓	✓	✓		
BRISTOL BUCKS CO	DR WAGNERS HOSP 435 RADCLIFFE ST	ALL	✓				✓
BRISTOL BUCKS CO	V D CONTROL CLINIC COMMUNITY HOUSE	ALL	✓	✓	✓		
BROWNSVILLE FAYETTE CO	BROWNSVILLE HOSPITAL	ALL	✓	✓	✓		
BRYN MAWR MONTGOMERY CO	BRYN MAWR HOSPITAL	ALL	✓			✓	
BURGETTSTOWN WASHINGTON CO	STATE V D CLINIC MINERS HALL	ALL	✓	✓	✓		
BUTLER BUTLER CO	V D CLINIC COMMUNITY BUILDING	ALL	✓	✓	✓		
CARBONDALE LACKAWANNA CO	ST JOS HOSP CLINIC ST JOSEPHS HOSPITAL	ALL	✓	✓	✓		
CARLISLE CUMBERLAND CO	CARLISLE HOSPITAL	ALL	✓	✓	✓		
CHAMBERSBURG FRANKLIN CO	CHAMBERSBURG HOSP	ALL	✓	✓	✓		
CHESTER DELAWARE CO	CHESTER HOSPITAL 1908 WEST THIRD ST	ALL	✓	✓	✓	✓	
CHESTER DELAWARE CO	STATE CLINIC 400 EAST 8TH ST	ALL	✓	✓	✓		
CLEARFIELD CLEARFIELD CO	CLEARFIELD HOSPITAL	ALL	✓	✓	✓		
COATESVILLE CHESTER CO	STATE V D CLINIC 260 EAST MAIN ST	ALL	✓	✓	✓		
COLUMBIA LANCASTER CO	COLUMBIA HOSPITAL	ALL	✓	✓	✓		
CONNELSVILLE FAYETTE CO	STATE V D CLINIC 148 SO ARCH ST	ALL	✓	✓	✓		
CORRY ERIE CO	CITY CLINIC MUNICIPAL BLDG	ALL	✓	✓	✓		
DANVILLE MONTOUR CO	GEISINGER MEM HOSP	ALL	✓			✓	✓
DARBY DELAWARE CO	FITZG MERCY HOSP LANSDOWNE AVE	ALL	✓	✓		✓	
DREXEL HILL DELAWARE CO	DELAWARE CO HOSP LANSDOWNE AVE	ALL	✓	✓	✓		
DU BOIS CLEARFIELD CO	G U CLINIC 2 SOUTH MAIN ST	ALL	✓	✓	✓		

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PENNSYLVANIA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
EASTON NORTHAMPTON CO	EASTON HOSPITAL	ALL	✓	✓	✓		
ERIE ERIE CO	STATE CLINIC 2117 PEACH ST	ALL	✓	✓	✓		
FOUNTAIN SPRINGS SCHUYLKILL CO	STATE HOSPITAL	ALL	✓		✓	✓	
FRANKLIN VENANGO CO	FRANKLIN HOSP OISP	ALL	✓	✓	✓		
GETTYSBURG ADAMS CO	ANNIE M WARNER HOSP	ALL	✓	✓	✓		
GREENSBURG WESTMORELAND CO	CO HOSPITAL ASSN	ALL	✓	✓	✓		
HARRISBURG DAUPHIN CO	CITY CLINIC 1112 NORTH 6TH ST	ALL	✓	✓	✓		
HARRISBURG DAUPHIN CO	HARRISBURG HOSPITAL	ALL	✓	✓	✓	✓	
HARRISBURG DAUPHIN CO	POLYCLINIC HOSPITAL THIRD AND RAONOR STS	ALL	✓	✓	✓		
HAZLETON LUZERNE CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
HOMESTEAD ALLEGHENY CO	SYPHILIS CLINIC 100 EAST 8TH AVE	ALL	✓	✓	✓		
HUNTINGDON HUNTINGDON CO	STATE CLINIC 821 MIFFLIN ST	ALL	✓	✓	✓		
INDIANA INDIANA CO	STATE CLINIC 37 SO 9 STREET	ALL	✓	✓	✓		
JOHNSTOWN CAMBRIA CO	LEE HOSPITAL 320 MAIN ST	ALL	✓	✓	✓		
JOHNSTOWN CAMBRIA CO	STATE CLINIC 344 LINCOLN ST	ALL	✓	✓	✓		
KANE MCKEAN CO	V O CLINIC COMMUNITY HOSPITAL	ALL	✓	✓	✓		
KITTANNING ARMSTRONG CO	CITY CLINIC COURTHOUSE ANNEX	ALL	✓	✓	✓		
LANCASTER LANCASTER CO	LANCASTER GEN HOSP	ALL	✓	✓	✓		
LANCASTER LANCASTER CO	ST JOSEPH HOSPITAL 202 COLLEGE AVE	ALL	✓	✓	✓		
LATROBE WESTMORELAND CO	LATROBE HOSPITAL	ALL	✓	✓	✓		
LEBANON LEBANON CO	GENITO URINARY CLIN GOOD SAMARITAN HOSP	ALL	✓	✓	✓		
LEWISTOWN MIFFLIN CO	V O CLINIC 30 CHESTNUT ST	ALL	✓	✓	✓		
LOCK HAVEN CLINTON CO	V D CLINIC LOCK HAVEN HOSPITAL	ALL	✓	✓	✓		
MCKEESPORT ALLEGHENY CO	MCKEESPORT HOSPITAL 1501 5TH AVE	ALL	✓	✓	✓	✓	
MCKEES ROCKS ALLEGHENY CO	OHIO VALLEY HOSPITAL	ALL	✓	✓	✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
MEADVILLE CRAWFORD CO	STATE CLINIC COURTHOUSE	ALL	✓	✓	✓		
MIFFLINTOWN JUNIATA CO	G U CLINIC J V BANK BLDG	ALL	✓	✓	✓		
MILLERSBURG DAUPHIN CO	CITY CLINIC 403 UNION ST	ALL	✓	✓	✓		
MILLVALE ALLEGHENY CO	GENITO URINARY CLIN BOROUGH BLDG	ALL	✓	✓	✓		
MONESSEN WESTMORELAND CO	CITY CLINIC CITY BLDG	ALL	✓	✓	✓		
MT CARMEL NORTHUMBERLAND CO	CITY CLINIC VICTORIA BLDG	ALL	✓	✓	✓		
NANTICOKE LUZERNE CO	NANTICOKE STATE HOSP	ALL	✓			✓	
NEW CASTLE LAWRENCE CO	CITY CLINIC 11 EAST ST	ALL	✓	✓	✓		
NEW EAGLE WASHINGTON CO	CITY CLINIC MEMORIAL HOSPITAL	ALL	✓	✓	✓		
NEW KENSINGTON WESTMORELAND CO	CITY CLINIC 1156 4TH AVE	ALL	✓	✓	✓		
NORRISTOWN MONTGOMERY CO	V D CLINIC BASIN AND POWELL ST	ALL	✓	✓	✓		
OIL CITY VENANGO CO	CITY G U CLINIC OIL CITY HOSPITAL	ALL	✓	✓	✓		
OIL CITY VENANGO CO	STATE CLINIC VEACH BLDG	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	AM ONCOLOGIC HOSP 33RD AND POWELTON	ALL	✓		✓	✓	✓
PHILADELPHIA PHILA CO	BARTON DISPENSARY 21ST AND NO COLLEGE	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	BROAD ST HOSPITAL 733 SOUTH BROAD ST	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	CHESTNUT HILL HOSP 8835 GERMANTOWN AVE	F	✓	✓	✓	✓	✓
PHILADELPHIA PHILADELPHIA CO	CHILDRENS HOSP OPD 18TH AND BAINBRIDGE	C	✓	✓	✓		✓
PHILADELPHIA PHILA CO	COMMUNITY HOSPITAL 10TH AND CARPENTER	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	EPISCOPAL HOSPITAL FRONT AT LEHIGH AVE	ALL	✓		✓		✓
PHILADELPHIA PHILA CO	DOUGLAS HOSPITAL 1530 LOMBARD ST	ALL	✓	✓	✓		
PHILADELPHIA PHILADELPHIA CO	GEN HOSP V D CLINIC 3400 PINE ST	ALL	✓		✓		
PHILADELPHIA PHILADELPHIA CO	FRANKFORD HOSP O P D FRANKFORD AVE	ALL	✓	✓	✓	✓	
PHILADELPHIA PHILA CO	GERMANTOWN HOSPITAL PENN AND CHEW STS	ALL	✓	✓		✓	
PHILADELPHIA PHILA CO	GRAD HOSP CLINIC 18TH AND LOMBARD STS	ALL	✓	✓	✓	✓	

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PENNSYLVANIA

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
PHILADELPHIA PHILA CO	HAHNEMANN HOSPITAL BROAD ST ABOVE RACE	ALL	✓		✓	✓	
PHILADELPHIA PHILA CO	JEFFERSON HOSPITAL 10TH AND SANSOM STS	ALL	✓	✓	✓	✓	
PHILADELPHIA PHILA CO	JEWISH HOSPITAL YORK AND TABOR RO	ALL	✓	✓		✓	
PHILADELPHIA PHILA CO	KENSINGTON HOSP 136 WEST DRAMOND ST	F	✓	✓	✓	✓	✓
PHILADELPHIA PHILA CO	LANKENAU HOSPITAL GIRARD AT CORINTHIAN	C	✓	✓	✓	✓	✓
PHILADELPHIA PHILA CO	MEMORIAL HOSPITAL 5800 RIDGE AVE	ALL	✓	✓	✓	✓	✓
PHILADELPHIA PHILADELPHIA CO	MEMORIAL HOSPITAL ROXBOROUGH	ALL	✓		✓		✓
PHILADELPHIA PHILA CO	MERCY HOSPITAL 5000 WOODLAND AVE	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	METH EPISC HOSP BROAD AND WOLF STS	ALL	✓			✓	
PHILADELPHIA PHILA CO	MT SINAI HOSPITAL 5TH AND HEED STS	ALL	✓	✓	✓	✓	✓
PHILADELPHIA PHILA CO	NORTHEASTERN HOSP ALLEGHENY AT TULIP	ALL	✓	✓	✓	✓	✓
PHILADELPHIA PHILA CO	N LIBERTIES HOSP 7TH AND BROWN STS	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	PENNSYLVANIA HOSP 8TH AND SPRUCE STS	ALL	✓	✓	✓	✓	✓
PHILADELPHIA PHILA CO	PRESBYTERIAN HOSP 39TH ST AT POWELTON	ALL	✓	✓	✓	✓	✓
PHILADELPHIA PHILA CO	ST AGNES HOSPITAL BROAD AND MIFLIN STS	ALL	✓	✓		✓	
PHILADELPHIA PHILA CO	ST CHRISTOPHERS HOSP LAWRENCE ST	C	✓	✓	✓	✓	✓
PHILADELPHIA PHILADELPHIA CO	ST JOSEPHS HOSP 16TH ST AT GIRARD	ALL	✓	✓	✓		✓
PHILADELPHIA PHILA CO	ST LUKES HOSPITAL 8TH AND THOMPSON STS	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	ST MARYS HOSPITAL FRANKFORD AT PALMER	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	ST VINCENTS HOSP 70TH ST AT WOODLAND	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	SKIN AND CANCER HOSP 802 PINE ST	ALL	✓		✓	✓	✓
PHILADELPHIA PHILA CO	STATE CLINIC 1137 SOUTH 20TH ST	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	STATE CLINIC 1129 CALLOWHILL ST	ALL	✓	✓	✓		
PHILADELPHIA PHILADELPHIA CO	STETSON HOSPITAL 1745 NO 4TH ST	ALL	✓	✓	✓		✓
PHILADELPHIA PHILA CO	TEMPLE MED SCHOOL BROAD AND ONTARIO ST	ALL	✓			✓	

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
PHILADELPHIA PHILA CO	UNIV OF PENNA HOSP 34TH AND SPRUCE STS	ALL	✓			✓	✓
PHILADELPHIA PHILADELPHIA CO	V D CLINIC 20TH AND BERKS STS	ALL	✓	✓	✓		
PHILADELPHIA PHILA CO	WILLS EYE CLINIC SPRING GARDEN ST	ALL	✓		✓	✓	
PHILADELPHIA PHILADELPHIA CO	WOMENS COLLEGE HOSP	ALL	✓	✓	✓		
PHILADELPHIA PHILADELPHIA CO	WOMENS HOMEO HOSP SUSQUEHANNA AVE	ALL	✓	✓		✓	
PHILADELPHIA PHILADELPHIA CO	WOMANS HOSPITAL 4035 PARRISH ST	F	✓		✓	✓	✓
PHILIPSBURG CENTRE CO	STATE HOSPITAL 16 SOUTH FRONT ST	ALL	✓	✓	✓		
PHOENIXVILLE CHESTER CO	PHOENIXVILLE HOSP	ALL	✓	✓	✓		
PITTSBURGH ALLEGHENY CO	ALLEGHENY GEN HOSP 320 EAST NORTH AVE	ALL	✓	✓	✓	✓	
PITTSBURGH ALLEGHENY CO	BELVEDERE HOSPITAL 801 PAULSON AVE	ALL	✓	✓	✓		
PITTSBURGH ALLEGHENY	CENTRAL DIAG CLINIC	ALL	✓		✓		
PITTSBURGH ALLEGHENY CO	CHILDRENS HOSPITAL 127 DE SOTA ST	C	✓		✓	✓	
PITTSBURGH ALLEGHENY CO	FALK CLINIC 3601 FIFTH AVE	A	✓	✓	✓	✓	
PITTSBURGH ALLEGHENY CO	HEALTH CLINIC 2405 CENTER AVE	N	✓	✓	✓		
PITTSBURGH ALLEGHENY CO	HOSPITALS ASSN FRANKSTOWN AVE	ALL	✓	✓		✓	
PITTSBURGH ALLEGHENY CO	MAGEE HOSPITAL FORBES AT HALKET ST	ALL	✓		✓		
PITTSBURGH ALLEGHENY CO	MERCY HOSPITAL PRIDE AND LOCUST STS	ALL	✓		✓	✓	
PITTSBURGH ALLEGHENY CO	MONTEFIORE HOSPITAL 3459 FIFTH AVE	ALL	✓	✓	✓		
PITTSBURGH ALLEGHENY CO	PASSAVANT DISPENSARY ROBERTS AND REED STS	ALL	✓	✓	✓	✓	
PITTSBURGH ALLEGHENY CO	ST FRANCIS HOSP FORTY FIFTH ST	ALL	✓	✓	✓		
PITTSBURGH ALLEGHENY CO	ST JOHNS GEN HOSP 3339 MCCLURE AVE N S	ALL	✓		✓		
PITTSBURGH ALLEGHENY CO	ST MARGARET MEM HOSP 46TH ST	ALL	✓	✓	✓		
PITTSBURGH ALLEGHENY CO	SHADYSIDE CLINIC CENTER AVE	ALL	✓	✓	✓		
PITTSBURGH ALLEGHENY CO	SKIN AND CANCER FDN 4518 WINTHROP ST	ALL	✓		✓	✓	
PITTSBURGH ALLEGHENY CO	SOUTH SIDE HOSPITAL SOUTH 20TH ST	ALL	✓	✓	✓		

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PENNSYLVANIA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
PITTSBURGH ALLEGHENY CO	WESTERN PENNA HOSP FRIENDSHIP AVE	ALL	✓	✓	✓		
PITTSTON LUZERNE CO	PITTSTON HOSPITAL	ALL	✓		✓		
POINT MARION FAYETTE CO	CITY CLINIC MUNICIPAL BLDG	ALL	✓	✓	✓		
POTTSTOWN MONTGOMERY CO	POTTSTOWN HOSPITAL	ALL	✓	✓	✓		
POTTSVILLE SCHUYLKILL CO	POTTSVILLE HOSPITAL	ALL	✓	✓	✓	✓	
PUNXSUATAWNEY JEFFERSON CO	STATE CLINIC MINER TRUST BLDG	ALL	✓	✓	✓		
QUAKERTOWN BUCKS CO	COMMUNITY HOSPITAL 11TH ST AND PARK AVE	ALL	✓	✓	✓		
READING BERKS CO	HOMEOPATHIC HOSPITAL 135 NORTH 6TH ST	ALL	✓	✓	✓	✓	
READING BERKS CO	ST JOSEPHS HOSPITAL 12TH AND WALNUT STS	ALL	✓	✓		✓	
RENOVO CLINTON CO	RENOVO HOSP ANNEX BONAUGH BUILDING	ALL	✓	✓	✓		
RIDLEY PARK DELAWARE CO	TAYLOR HOSPITAL	ALL	✓		✓		
ROCHESTER BEAVER CO	ROCHESTER GEN HOSP	ALL	✓	✓	✓		
SAYRE BRADFORD CO	ROBERT PACKER HOSP	ALL	✓	✓	✓	✓	
SCRANTON LACKAWANNA CO	HAHNEMANN HOSP OPD 316 COLFAX AVE	ALL	✓	✓	✓	✓	
SCRANTON LACKAWANNA CO	ST JOS CH MAT HOSP	ALL	✓	✓	✓		
SCRANTON LACKAWANNA CO	STATE CLINIC 331 ADAMS AVE	ALL	✓	✓	✓		
SEWICKLEY ALLEGHENY CO	VALLEY HOSPITAL BLACKBURN RD	ALL	✓	✓	✓		
SHAMOKIN NORTHUMBERLAND CO	STATE CLINIC 525 NORTH MARKET ST	ALL	✓	✓	✓		
SHARON MERCER CO	C H BUHL HOSPITAL	ALL	✓	✓	✓		
SHENANDOAH SCHUYLKILL CO	STATE CLINIC MAIN AND LLOYD ST	ALL	✓	✓	✓		
SOMERSET SOMERSET CO	V D CLINIC NATIONAL BANK BLDG	ALL	✓	✓	✓		
SPANGLER CAMBRIA CO	MINERS HOSPITAL	W	✓	✓	✓		
STROUDSBURG MONROE CO	CITY CLINIC 13 NORTH 6TH ST	ALL	✓	✓	✓		
SUNBURY NORTHUMBERLAND CO	STATE CLINIC 26 NORTH 4TH ST	ALL	✓	✓	✓		
TYRONE BLAIR CO	CITY CLINIC LOGAN AVE AT 11TH ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
UNIONTOWN FAYETTE CO	UNIONTOWN HOSPITAL WEST BERKELEY ST	ALL	✓	✓	✓		
WARREN WARREN CO	GENITO URINARY CLIN 208 THIRD STREET	ALL	✓	✓	✓		
WASHINGTON WASHINGTON CO	WASHINGTON HOSP	ALL	✓	✓	✓		
WAYNESBORO FRANKLIN CO	WAYNESBORO HOSPITAL	ALL	✓	✓	✓		
WAYNESBURG GREENE CO	V D CLINIC 25 EAST HIGH ST	ALL	✓	✓	✓		
WELLSBORO TIOGA CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
WEST CHESTER CHESTER CO	HOMEOPATHIC HOSPITAL	ALL	✓	✓	✓		
WEST READING BERKS CO	READING CLINIC	ALL	✓		✓	✓	
WILKES BARRE LUZERNE CO	GENERAL HOSPITAL NORTH RIVER ST	ALL	✓	✓	✓	✓	✓
WILKES BARRE LUZERNE CO	KIRBY HEALTH CENTER 71 NORTH FRANKLIN ST	ALL	✓	✓	✓		
WILKES BARRE LUZERNE CO	MERCY HOSPITAL 196 HANOVER ST	ALL	✓	✓	✓	✓	✓
WILKINSBURG ALLEGHENY CO	COLUMBIA HOSPITAL 312 WEST ST	ALL	✓		✓	✓	
WILLIAMSPORT LYCOMING CO	STATE CLINIC 625 WEST EDWIN ST	ALL	✓	✓	✓		
WINDBER SOMERSET CO	BERWIND CLINIC WINDBER HOSPITAL	ALL	✓	✓	✓		✓
YORK YORK CO	YORK HOSPITAL	ALL	✓	✓	✓		
	RHODE ISLAND						
BRISTOL BRISTOL CO	SE HEALTH UNIT ROCKWELL HOUSE	ALL	✓		✓		
NEWPORT NEWPORT CO	NEWPORT HOSPITAL FRIENDSHIP ST	ALL	✓	✓		✓	
PAWTUCKET PROVIDENCE CO	MEMORIAL HOSPITAL PROSPECT ST	ALL	✓	✓	✓	✓	
PROVIONECE PROVIOENCE CO	C V CHAPIN HOSP 153 EATON ST	ALL	✓	✓	✓	✓	
PROVIOENCE PROVIOENCE CO	RHOOE ISLANO HOSP 593 EOOY ST	ALL	✓	✓		✓	
PROVIOENCE PROVIOENCE CO	ST JOSPEH HOSPITAL BROAD ANU PEACE STS	ALL	✓	✓	✓	✓	✓
WAKEFIELO WASHINGTON CO	SOUTH COUNTY HOSP	ALL	✓		✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
WICKFORD WASHINGTON CO	VISITING NURSES HEADQUARTERS	ALL	✓		✓		
WOONSOCKET PROVIDENCE CO	WOONSOCKET HOSPITAL CASS AVE	ALL	✓	✓	✓	✓	
	SOUTH CAROLINA						
ABBEVILLE ABBEVILLE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓	✓	
ADAMS RUN CHARLESTON CO	CHARLESTON CO MOBILE LEGARE	ALL	✓	✓	✓		
ADAMS RUN CHARLESTON CO	V D CLINIC HARMON BLDG	ALL	✓	✓	✓		
AIKEN AIKEN CO	COUNTY HEALTH DEPT AGRICULTURAL BLDG	ALL	✓		✓		
ALLENDALE ALLENDALE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
ANDERSON ANDERSON CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓	✓	
ANDREWS GEORGETOWN CO	V D CLINIC MASONIC BLDG	ALL	✓	✓	✓		
AWENDAW CHARLESTON CO	CHARLESTON CO MOBILE BUCK HALL	ALL	✓	✓	✓		
AWENDAW CHARLESTON CO	CHARLESTON CO MOBILE FREEMANS STORE 15 MI	ALL	✓	✓	✓		
AWENDAW CHARLESTON CO	CHARLESTON CO MOBILE THAMES STORE 24 MI	ALL	✓	✓	✓		
AWENDAW CHARLESTON CO	CHARLESTON CO MOBILE THOMAS STORE 12 MI	ALL	✓	✓	✓		
BALLENTINE RICHLAND CO	COUNTY V D CLINIC STPETERS CHURCH	ALL	✓	✓	✓		
BAMBERG BAMBERG CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓	✓	
BARNWELL BARNWELL CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓	✓	
BATESBURG LEXINGTON CO	V D CLINIC TOWN HALL	ALL	✓	✓	✓		
BEAUFORT BEAUFORT CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
BENNETTSVILLE MARLBORO CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
BETHUNE KERSHAW CO	COUNTY HEALTH DEPT HOUSEKPG AIDE CENTER	ALL	✓	✓	✓		
BIG STATE BEAUFORT CO	BEAUFORT CO MOBILE SOCIETY HALL	ALL	✓	✓	✓		
BISHOPVILLE LEE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓	✓	

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
BLANEY KERSHAW CO	COUNTY HEALTH DEPT WHITE HIGH SCHOOL	ALL	✓	✓	✓		
BLUFFTON BEAUFORT CO	COUNTY HEALTH DEPT MEDICAL CENTER	ALL	✓	✓	✓		
BLYTHEWOOD RICHLAND CO	V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
CAMDEN KERSHAW CO	COUNTY HEALTH DEPT AGRICULTURAL BLDG	ALL	✓	✓	✓		
CARLISLE UNION CO	COUNTY HEALTH DEPT COLORED SCHOOL	ALL	✓	✓	✓		
CHARLESTON CHARLESTON CO	CHARLESTON CO MOBILE HEALTH DEPARTMENT	ALL	✓	✓	✓		
CHARLESTON CHARLESTON CO	HEALTH CENTER CLINIC HEALTH DEPT	ALL	✓	✓	✓		
CHARLESTON CHARLESTON CO	NEGRO HOSP CLINIC 135 CANNON ST	ALL	✓	✓	✓		
CHARLESTON CHARLESTON CO	CO HEALTH CENTER OLD CITADEL	ALL	✓	✓	✓		
CHARLESTON CHARLESTON CO	ROPER HOSPITAL DISP LUCAS AND CALHOUN	ALL	✓	✓	✓		
CHERAW CHESTERFIELD CO	COUNTY HEALTH CENTER	ALL	✓	✓	✓		
CHESTER CHESTER CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓	✓	
CHESTERFIELD CHESTERFIELD CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
CLEMSON PICKENS CO	V D CLINIC MASONIC BLDG	ALL	✓	✓			✓
CLINTON LAURENS CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓	✓	
CLIO MARLBORO CO	CO HEALTH OFFICE	ALL	✓	✓	✓		
COLUMBIA RICHLAND CO	COUNTY V D CLINIC 1209 LADY ST	ALL	✓	✓	✓		
CONWAY HORRY CO	COUNTY HEALTH DEPT COMMUNITY CENTER	ALL	✓	✓		✓	
CROSS BERKELEY CO	COUNTY HEALTH DEPT JEHOVAH CHURCH	ALL	✓	✓	✓		
CROSS HILL LAURENS CO	CITY CLINIC HEALTH CENTER						
DARLINGTON DARLINGTON CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓	✓	
DENMARK BAMBERG CO	V D CLINIC CO HEALTH CENTER	ALL	✓		✓	✓	
DILLON DILLON CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓	✓	
DONALDS ABBEVILLE CO	COUNTY V D CLINIC COLORED SCHOOL	ALL	✓	✓	✓		
EASLEY PICKENS CO	V D CLINIC WALKERMOORE MORTUARY	ALL	✓	✓	✓	✓	

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SOUTH CAROLINA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
EASTOVER RICHLAND CO	V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
EDGEFIELD EDGEFIELD CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
EDISTO ISLAND CHARLESTON CO	CHARLESTON CO MOBILE POSNERS STORE	ALL	✓	✓	✓		
ESTILL HAMPTON CO	COUNTY HEALTH DEPT TOWN HALL	ALL	✓	✓	✓		
FLORENCE FLORENCE CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓	✓	
FORT MILL YORK CO	COUNTY HEALTH DEPT BRANCH HEALTH OFFICE	ALL	✓		✓		
FORT MOTTE CALHOUN CO	COUNTY HEALTH DEPT MURRAYS STORE	ALL	✓	✓	✓		
FOUNTAIN INN GREENVILLE CO	COUNTY HEALTH DEPT KELLETT BLDG	ALL	✓	✓	✓	✓	
GAFFNEY CHEROKEE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
GARNETT HAMPTON CO	V D CLINIC BRIGHTON COL SCHOOL	N	✓	✓	✓		
GEORGETOWN GEORGETOWN CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
GOOD HOPE BEAUFORT CO	BEAUFORT CO MOBILE GOOD HOPE COL SCHOOL	N	✓	✓	✓		
GREELYVILLE WILLIAMSBURG CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓	✓	✓	✓	
GREEN POND COLLETON CO	COLLETON CO MOBILE CLINIC BLDG	ALL	✓		✓		
GREENVILLE GREENVILLE CO	CITY CLINIC CITY HALL MAIN ST	ALL	✓	✓		✓	
GREENVILLE GREENVILLE CO	GENERAL HOSP CLINIC	ALL	✓	✓			
GREENVILLE GREENVILLE CO	COUNTY V D CLINIC 13 WEST COURT ST	ALL	✓	✓	✓	✓	
GREENWOOD GREENWOOD CO	COUNTY HEALTH DEPT 515 MAIN ST	ALL	✓	✓	✓		
HAMPTON HAMPTON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
HARDEEVILLE JASPER CO	COUNTY CLINIC MOBILE CITY HALL	ALL	✓	✓	✓		
HARTSVILLE DARLINGTON CO	COUNTY CLINIC COMMUNITY BLDG	ALL	✓	✓	✓	✓	
HEMINGWAY WILLIAMSBURG CO	V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
HILTONHEAD IS BEAUFORT CO	BEAUFORT CO MOBILE CHAPLIN SCHOOL BLDG	ALL	✓	✓	✓		
HOPKINS RICHLAND CO	V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
IRMO LEXINGTON CO	HEALTH CENTER	ALL	✓	✓	✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
JAMES ISLAND CHARLESTON CO	CHARLESTON CO MOBILE COKERS STORE	ALL	✓	✓	✓		
JOHNS ISLAND CHARLESTON CO	CHARLESTON CO MOBILE HEBRON CHURCH	ALL	✓	✓	✓		
JOHNS ISLAND CHARLESTON CO	CHARLESTON CO MOBILE HOWELLS STORE	ALL	✓	✓	✓		
JOHNS ISLAND CHARLESTON CO	CHARLESTON CO MOBILE LIMEHOUSE STORE	ALL	✓	✓	✓		
JOHNS ISLAND CHARLESTON CO	CHARLESTON CO MOBILE REO TOP STORE	ALL	✓	✓	✓		
JOHNS ISLAND CHARLESTON CO	CHARLESTON CO MOBILE TUCKERS STORE	ALL	✓	✓	✓		
JOHNSTON EDGEFIELD CO	COUNTY HEALTH DEPT COLORED SCHOOL HOUSE	N	✓	✓	✓		
KERSHAW LANCASTER CO	LANCASTER CO CLINIC KERSHAW COL SCHOOL	ALL	✓	✓	✓	✓	
KINGSTREE WILLIAMSBURG CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓	✓	
KINGVILLE RICHLAND CO	V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
LAKE VIEW DILLON CO	COUNTY HEALTH DEPT LAKE VIEW PHARMACY	ALL	✓	✓	✓	✓	
LAMAR DARLINGTON CO	COUNTY V D CLINIC OR GARY BOYKINS OFC	ALL	✓	✓	✓	✓	
LANCASTER LANCASTER CO	COUNTY HEALTH DEPT COUNTY OFFICE BLDG	ALL	✓	✓	✓	✓	
LATTA DILLON CO	COUNTY CLINIC HAYES GROCERY STORE	ALL	✓	✓	✓	✓	
LAURENS LAURENS CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
LEVY BEAUFORT CO	BEAUFORT CO MOBILE ZION SOCIETY HALL	ALL	✓	✓	✓		
LEXINGTON LEXINGTON CO	COUNTY HEALTH DEPT AGRICULTURAL BLDG	ALL	✓		✓		
LIBERTY HILL CHARLESTON CO	CHARLESTON CO MOBILE COLORED SCHOOL	ALL	✓	✓	✓		
LONE STAR CALHOUN CO	COUNTY HEALTH DEPT WEEKS STORE	ALL	✓	✓	✓	✓	
LORIS HORRY CO	COUNTY HEALTH DEPT GATEWAY DRUG CO	ALL	✓	✓		✓	
LOUNDSVILLE ABBEVILLE CO	COUNTY V D CLINIC BRICK STORE	ALL	✓	✓	✓		
LOWRYS CHESTER CO	COUNTY HEALTH DEPT	N	✓	✓	✓		
LYNCHBURG LEE CO	COUNTY HEALTH DEPT BANK BLDG	ALL	✓	✓	✓		
MCCLELLANVILLE CHARLESTON CO	CHARLESTON CO MOBILE MR BECKMANS OFFICE	ALL	✓	✓	✓		
MCCOLL MARLBORO CO	CO HEALTH DEPT	ALL	✓	✓	✓		

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SOUTH CAROLINA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
MC CORMICK MCCORMICK CO	COUNTY HEALTH OEPT COURTHOUSE	ALL	✓	✓	✓		
MANNING CLARENOON CO	COUNTY HEALTH OEPT COURTHOUSE	ALL	✓	✓	✓		
MARION MARION CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓	✓	
MARTINS ALLENDALE CO	V D CLINIC STORE BLDG	ALL	✓	✓	✓		
MARTINS POINT CHARLESTON CO	COUNTY V D CLINIC JERUSALEM CHURCH	ALL	✓	✓	✓		
MEGGETTS CHARLESTON CO	CHARLESTON CO MOBILE ANIVESTER CHURCH	ALL	✓	✓	✓		
MIOLANO PARK CHARLESTON CO	CHARLESTON CO MOBILE STALLS STORE	ALL	✓	✓	✓		
MONCKS CORNER BERKELEY CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
MT PLEASANT CHARLESTON CO	CHARLESTON CO MOBILE 4 MILE CHURCH	ALL	✓	✓	✓		
MULLINS MARION CO	COUNTY HEALTH OEPT HAROWARE STORE	ALL	✓	✓	✓	✓	
MYERS CHARLESTON CO	CHARLESTON CO MOBILE HACKERMANNS STORE	ALL	✓	✓	✓		
MYRTLE BEACH HORRY CO	COUNTY V O CLINIC COLOREO SCHOOL	N	✓	✓	✓		
NEWBERRY NEWBERRY CO	COUNTY HEALTH OEPT EXCHANGE BANK BLOG	ALL	✓		✓		
ORANGEBURG ORANGEBURG CO	COUNTY HEALTH DEPT CO OFFICE BLOG	ALL	✓	✓	✓		
PAGELANO CHESTERFIELD CO	CO HEALTH OEPT	ALL	✓	✓	✓		
PARKERS FERRY CHARLESTON CO	CHARLESTON CO MOBILE CROSS ROAOS	ALL	✓	✓	✓		
PARRIS ISLANO BEAUFORT CO	COUNTY HEALTH OEPT STATION HOSPITAL	ALL	✓	✓	✓		
PAWLEYS ISLANO GEORGETOWN CO	COUNTY HEALTH DEPT NORRIS CLINIC	N	✓	✓	✓		
PICKENS PICKENS CO	V O CLINIC HEALTH OEPARTMENT	ALL	✓	✓	✓	✓	
PINEVILLE BERKELEY CO	COUNTY HEALTH OEPT REOEEMER CHURCH	ALL	✓	✓	✓		
PONTIAC RICHLANO CO	COUNTY V O CLINIC EXPERIMENT STATION	ALL	✓	✓	✓		
RANTOWLES CHARLESTON CO	CHARLESTON CO MOBILE PRATTS ESSO STATION	ALL	✓	✓	✓		
RAVENEL CHARLESTON CO	CHARLESTON CO MOBILE POST OFFICE	ALL	✓	✓	✓		
RICHBURG CHESTER CO	COUNTY HEALTH DEPT PLEASANT GROVE SCH	ALL	✓	✓	✓		
RIOGELANO JASPER CO	COUNTY HEALTH OEPT AGRICULTURAL BLOG	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TD *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
RIDGE SPRING SALUDA CO	COUNTY HEALTH CENTER	ALL	✓	✓	✓		
RUFFIN COLLETON CO	COUNTY HEALTH DEPT COLORED CHURCH	N	✓		✓		
ST GEORGE DORCHESTER CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
ST MATTHEWS CALHOUN CO	COUNTY HEALTH DEPT AGRICULTURAL BLDG	ALL	✓	✓	✓		
SALUDA SALUDA CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
SANTEE CHARLESTON CO	CHARLESTON CO MOBILE SOLOMONS STORE	ALL	✓		✓		
SENECA OCONEE CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
SHELDON BEAUFORT CO	BEAUFORT CO MOBILE CANAAN BAPT CHURCH	ALL	✓	✓	✓		
SOCIETY HILL DARLINGTON CO	COUNTY HEALTH DEPT DR TOWNSENDS OFFICE	ALL	✓	✓	✓	✓	
SPARTANBURG SPARTANBURG CO	CITY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
SPARTANBURG SPARTANBURG CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SPARTANBURG SPARTANBURG CO	SPARTANBURG GEN HOSP 891 NORTH CHURCH ST	ALL	✓	✓	✓		
SUMMERVILLE DORCHESTER CO	COUNTY HEALTH DEPT CITY BLDG	ALL	✓	✓	✓		
SUMTER SUMTER CO	CITY HEALTH DEPT 8 CALDWELL ST	ALL	✓	✓	✓	✓	
SUMTER SUMTER CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓	✓	
UNION UNION CO	COUNTY HEALTH DEPT KIRBY BLDG	ALL	✓	✓	✓	✓	
VAN WYCK LANCASTER CO	COUNTY HEALTH DEPT BRICK YARD OFFICE	ALL	✓	✓	✓	✓	
VARNVILLE HAMPTON CO	COUNTY HEALTH DEPT HEALTH CENTER	ALL	✓	✓	✓		
WAOMALAW CHARLESTON CO	CHARLESTON CO MOBILE BETHLEHEM BAP CHURCH	ALL	✓	✓	✓		
WAGENER AIKEN CO	COUNTY HEALTH DEPT CORBELTS OFFICE BLDG	ALL	✓		✓		
WALHALLA OCONEE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
WALTERBORO COLLETON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
WANDO BERKELEY CO	COUNTY HEALTH DEPT ST STEPHENS CHURCH	ALL	✓	✓	✓		
WEST COLUMBIA LEXINGTON CO	COUNTY HEALTH DEPT TOWN HALL	ALL	✓	✓	✓		
WESTMINISTER OCONEE CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
WINNSBORO FAIRFIELD CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓		✓		
WOODRUFF SPARTANBURG CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
YEMASSEE HAMPTON CO	HAMPTON CO MOBILE COLORED SCHOOL BLDG	N	✓	✓	✓		
YORK YORK CO	CO HEALTH DEPT	ALL	✓	✓	✓		
	SOUTH DAKOTA **						
SIOUX FALLS MINNEHAHA CO	CITY HEALTH DEPT	ALL	✓	✓	✓		
	TENNESSEE						
ALAMO CROCKETT CO	COUNTY CLINIC	ALL	✓	✓	✓		
ARLINGTON SHELBY CO	SHELBY CO MOBILE ARLINGTON DEPOT	W	✓	✓	✓		
ARLINGTON SHELBY CO	SHELBY CO MOBILE S Y WILSONS STORE	N	✓	✓	✓		
ATHENS MCMINN CO	COUNTY HEALTH UNIT COURTHOUSE	ALL	✓	✓	✓		
BAILEY SHELBY CO	CO MOBILE UNIT POST OFFICE	N	✓	✓	✓		
BAKEWELL HAMILTON CO	HEALTH CENTER	ALL	✓	✓	✓		
BARRETVILLE SHELBY CO	SHELBY CO MOBILE BARRETS STORE	N	✓	✓	✓		
BARTLETT SHELBY CO	SHELBY CO MOBILE UNDERTAKERS PARLOR	N	✓	✓	✓		
BELLS CROCKETT CO	COUNTY CLINIC OVER CHOCKETT BANK	ALL	✓	✓	✓		
BENJESTOWN SHELBY CO	SHELBY CO MOBILE BENJESTOWN COL SCH	N	✓	✓	✓		
BERCLAIR SHELBY CO	SHELBY CO MOBILE COMMUNITY CENTER	N	✓	✓	✓		
BETHLEHEM SHELBY CO	CO MOBILE UNIT COLORED SCHOOL	N	✓	✓	✓		
BLOUNTVILLE SULLIVAN CO	COUNTY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
BOLIVAR HARDEMAN CO	V D CLINIC COUNTY HEALTH UNIT	ALL	✓	✓	✓		

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** IN ADDITION TO CLINICS LISTED, THE ADDRESSES OF PHYSICIANS GIVING TREATMENT FOR VENEREAL DISEASES UNDER THE STATE PLAN MAY BE OBTAINED FROM STATE, COUNTY, AND MUNICIPAL OFFICERS.

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
BOLTON SHELBY CO	SHELBY CO MOBILE PEARLIES STORE	ALL	✓	✓	✓		
BRIDGEWATER SHELBY CO	SHELBY CO MOBILE BRIDGEWATER COL SCH	N	✓	✓	✓		
BRISTOL SULLIVAN CO	COUNTY CLINIC K M M HOSP	ALL	✓	✓	✓		
BRUNSWICK SHELBY CO	SHELBY CO MOBILE COLOREO SCHOOL	N	✓	✓	✓		
BYROSTOWN PICKETT CO	COUNTY HEALTH OEPT COURT HOUSE	ALL	✓	✓	✓		
CAPLEVILLE SHELBY CO	SHELBY CO MOBILE STORE	N	✓	✓	✓		
CELINA CLAY CO	COUNTY CLINIC	ALL	✓	✓	✓		
CENTERVILLE HICKMAN CO	COUNTY CLINIC RUSSELL BLDG	ALL	✓	✓	✓		
CHATTANOOGA HAMILTON CO	COURT DIAG CLINIC CITY HALL	ALL	✓	✓	✓		
CHATTANOOGA HAMILTON CO	BETHLEHEM HOUSE	N	✓	✓	✓		
CHATTANOOGA HAMILTON CO	COUNTY HEALTH DEPT						
CHATTANOOGA HAMILTON CO	GOOOWILL H CENTER	ALL	✓	✓	✓		
CHATTANOOGA HAMILTON CO	THOMPSON HOSP GLENWOOO ORIVE	C	✓		✓		
CHATTANOOGA HAMILTON CO	V O CLINIC ERLANGER HOSPITAL	A	✓	✓	✓		
CLARKSVILLE MONTGOMERY CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
CLEVELANO BRAOLEY CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
CLINTON ANOERSON CO	V O CLINIC 106 BROAD ST	ALL	✓	✓	✓		
COLLEGE GROVE WILLIAMSON CO	COUNTY HEALTH OEPT DEPOT	ALL	✓	✓	✓		
COLLIERVILLE SHELBY CO	COUNTY CLINIC	ALL	✓	✓	✓		
COLUMBIA MAURY CO	COUNTY HEALTH OEPT COURTHOUSE	ALL	✓	✓	✓		
COROOVA SHELBY CO	SHELBY CO MOBILE COROOVA OEPOT	ALL	✓	✓	✓		
COVINGTON TIPTON CO	V O CLINIC CO HEALTH OEPT	ALL	✓	✓	✓		
CROSSVILLE CUMBERLANO CO	COUNTY V O CLINIC	ALL	✓	✓	✓		
CUBA SHELBY CO	SHELBY CO MOBILE SIGLERS STORE	N	✓	✓	✓		
DANDRIDGE JEFFERSON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		

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TENNESSEE

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
DAYTON RHEA CO	COUNTY CLINIC	ALL	✓	✓	✓		
DECATUR MEIGS CO	COUNTY CLINIC	ALL	✓	✓	✓		
DECATURVILLE DECATUR CO	DISTRICT HEALTH DEPT	ALL	✓	✓	✓		
DRESDEN WEAKLEY CO	COUNTY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
DUNLAP SEQUATCHIE CO	COUNTY CLINIC	ALL	✓	✓	✓		
DYER GIBSON CO	COUNTY CLINIC SCHOOL BASEMENT	ALL	✓	✓	✓		
DYERSBURG DYER CO	COUNTY CLINIC 713 ELM ST	ALL	✓	✓	✓		
EADS SHELBY CO	SHELBY CO MOBILE RICHMONDS STORE	N	✓	✓	✓		
ELIZABETHTON CARTER CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
ELLENDALE SHELBY CO	SHELBY CO MOBILE FULLVIEW CHURCH	N	✓	✓	✓		
ELLENDALE SHELBY CO	SHELBY CO MOBILE HERRINGS STORE	W	✓	✓	✓		
ERIN HOUSTON CO	V D CLINIC OVER DRUG STORE	ALL	✓	✓	✓		
ERWIN UNICOI CO	COUNTY CLINIC 102 TUCKER ST	ALL	✓	✓	✓		
ERWIN UNICOI CO	ROCKY FORK CLINIC PRES MISSION DIS	ALL	✓	✓	✓		
ETOWAH MCMINN CO	COUNTY HEALTH DEPT LIBRARY	ALL	✓	✓	✓		
FAIRVIEW WILLIAMSON CO	HEALTH CENTER HWY 100 SO OF SCHOOL	ALL	✓	✓	✓		
FAYETTEVILLE LINCOLN CO	COUNTY HEALTH DEPT NORTH ELK AVE	ALL	✓	✓	✓		
FISHERVILLE SHELBY CO	SHELBY CO MOBILE BRIGGS STORE	N	✓	✓	✓		
FOREST HILL SHELBY CO	SHELBY CO MOBILE COLORED SCHOOL	N	✓	✓	✓		
FOREST HILL SHELBY CO	SHELBY CO MOBILE KINGS STORE	W	✓	✓	✓		
FRANKLIN WILLIAMSON CO	COUNTY HEALTH DEPT 3RD AVENUE SOUTH	ALL	✓	✓	✓		
FRIENDSHIP CROCKETT CO	COUNTY CLINIC REAR OF BANK BLDG	ALL	✓	✓	✓		
GAINESBORO JACKSON CO	COUNTY CLINIC	ALL	✓	✓	✓		
GALLATIN SUMNER CO	COUNTY HEALTH DEPT 107 FRANKLIN ST	ALL	✓	✓	✓		
GEETER SHELBY CO	SHELBY CO MOBILE GEETER COLORED SCH	N	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
GERMANTOWN SHELBY CO	SHELBY CO MOBILE GERMANTOWN DEPOT	ALL	✓	✓	✓		
GREENEVILLE GREENE CO	V D CLINIC CO HEALTH DEPT	ALL	✓	✓	✓		
GREENFIELD WEAKLEY CO	COUNTY CLINIC GROOMS HERRON BLDG	ALL	✓	✓	✓		
HACKS CROSS ROAD SHELBY CO	SHELBY CO MOBILE HACKS CROSS ROAD	ALL	✓	✓	✓		
HALLS LAUDERDALE CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
HAMNERS SHELBY CO	SHELBY CO MOBILE HAMNERS STORE	N	✓	✓	✓		
HARTSVILLE TROUSDALE CO	COUNTY CLINIC LIPSCOMB BLDG	ALL	✓	✓	✓		
HENDERSONVILLE SUMNER CO	COUNTY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
HILDERBRANDS SHELBY CO	CO MOBILE UNIT	N	✓	✓	✓		
HIXSON HAMILTON CO	HEALTH CENTER	ALL	✓	✓	✓		
HOWEVER SHELBY CO	CO MOBILE UNIT HOWEVER STORE	N	✓	✓	✓		
HUMBOLOT GIBSON CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
HUNTINGOON CARROLL CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
JACKSON MADISON CO	COUNTY HEALTH DEPT CHESTER AT LIBERTY	ALL	✓	✓	✓		
JAMESTOWN FENTRESS CO	COUNTY V D CLINIC	ALL	✓	✓	✓		
JEFFERSON CITY JEFFERSON CO	HEALTH CENTER ZINC MINE INFIRMARY	ALL	✓	✓	✓		
JELLICO CAMPBELL CO	V D CLINIC CITY HALL	ALL	✓	✓	✓		
JOHNSON CITY WASHINGTON CO	COUNTY CLINIC MUNICIPAL BLDG	ALL	✓	✓	✓		
JONESBORO WASHINGTON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
KENTON GIBSON CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
KERRVILLE SHELBY CO	SHELBY CO MOBILE BETHLEHEM COL SCH	N	✓	✓	✓		
KINGSPORT SULLIVAN CO	COUNTY CLINIC H V C HOSP	ALL	✓	✓	✓		
KINGSTON ROANE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓		✓		
KNOXVILLE KNOX CO	CAMP HOME 702 EAST JACKSON	F A	✓	✓	✓		
KNOXVILLE KNOX CO	COUNTY CLINIC 400 W HILL ST	ALL	✓	✓	✓		

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TENNESSEE

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
KNOXVILLE KNOX CO	V D CLINIC 619 WEST CLINCH ST	W	✓	✓	✓		
KNOXVILLE KNOX CO	V D CLINIC 211 STATE ST	N	✓	✓	✓		
KNOXVILLE KNOX CO	JUVENILE HOME MIDDLEBROOK PIKE	C	✓	✓	✓		
LAFOLLETTE CAMPBELL CO	COUNTY CLINIC TENNESSEE AVE	ALL	✓	✓	✓		
LEBANON WILSON CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
LEWISBURG MARSHALL CO	COUNTY HEALTH DEPT NORTH 1ST AVE	ALL	✓	✓	✓		
LEXINGTON HENDERSON CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
LIVINGSTON OVERTON CO	COUNTY HEALTH DEPT BOHANNAN HALL	ALL	✓	✓	✓		
LOCKE SHELBY CO	SHELBY CO MOBILE GAYDENS STORE	ALL	✓	✓	✓		
LUCY SHELBY CO	SHELBY CO MOBILE SYKES STORE	ALL	✓	✓	✓		
MCMINNVILLE WARREN CO	COUNTY HEALTH DEPT MONTGOMERY BLDG						
MADISONVILLE MONROE CO	COUNTY CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
MANCHESTER COFFEE CO	V D CLINIC HEALTH DEPT OFFICE	ALL	✓	✓	✓		
MARTIN WEAKLEY CO	COUNTY CLINIC MILANS DRUG STORE	ALL	✓	✓	✓		
MARYVILLE BLOUNT CO	COUNTY HEALTH DEPT GAMBLE BLDG	ALL	✓	✓	✓		
MASON TIPTON CO	V D CLINIC PORTER FUNERAL HOME	ALL	✓	✓	✓		
MEDINA GIBSON CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
MEMPHIS SHELBY CO	WELLINGTON CLINIC AT LINDEN STREET	N	✓	✓	✓		
MEMPHIS SHELBY CO	DOUGLAS V D CLINIC DOUGLAS SCHOOL	N	✓	✓	✓		
MEMPHIS SHELBY CO	JOHN GASTON HOSPITAL 879 MADISON	ALL	✓	✓	✓		
MEMPHIS SHELBY CO	NORTH MEMPHIS CLINIC MANASSAS HIGH SCHOOL	N	✓	✓	✓		
MEMPIS SHELBY CO	SHELBY CO HOSPITAL ROUTE 6	A	✓	✓	✓		
MEMPHIS SHELBY CO	S MEMPHIS H CENTER 1115 S 3RD ST	ALL	✓	✓	✓		
MILAN GIBSON CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
MILLINGTON SHELBY CO	SHELBY CO MOBILE HARRELLS STORE	W	✓	✓	✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
MILLINGTON SHELBY CO	SHELBY CO MOBILE HARRELLS STORE	W	✓	✓	✓		
MILLINGTON SHELBY CO	SHELBY CO MOBILE COLORED SCHOOL	N	✓	✓	✓		
MORRISTOWN HAMBLEN CO	COUNTY HEALTH DEPT MAIN ST	ALL	✓	✓	✓		
MOSCOW FAYETTE CO	COUNTY CLINIC OR FEEMSTERS OFFICE	ALL	✓	✓	✓		
MOUNTAIN CITY JOHNSON CO	COUNTY CLINIC	ALL	✓	✓	✓		
MT PISGAH SHELBY CO	SHELBY CO MOBILE MT PISGAH COL SCH	N	✓	✓	✓		
MURFREESBORO RUTHERFORO CO	RUTHERFORD HOSPITAL	ALL	✓	✓	✓		
NASHVILLE OAVIDSON CO	COUNTY HEALTH OEPT COURTHOUSE	ALL	✓	✓	✓		
NASHVILLE OAVIDSON CO	HUBBARD HOSPITAL 1005 18TH AVE NORTH	N	✓	✓		✓	
NASHVILLE DAVIDSON CO	STATE TR SCH CLINIC	ALL	✓	✓	✓		
NASHVILLE DAVIOSON CO	VANDERBILT UNIV HOSP 21ST AVE SOUTH	ALL	✓			✓	
NASHVILLE OAVIDSON CO	CITY CLINIC 2ND AVE AT LINDSLEY	ALL	✓	✓	✓		
NEWPORT COOKE CO	COUNTY CLINIC	ALL	✓	✓	✓		
NOLENSVILLE WILLIAMSON CO	COUNTY HEALTH DEPT HWY 11 AT MAIN ST	ALL	✓	✓	✓		
OAK GROVE SHELBY CO	SHELBY CO MOBILE OAKGROVE COL SCHOOL	N	✓	✓	✓		
OAKLAND FAYETTE CO	HEALTH CENTER DEPOT	ALL	✓	✓	✓		
OAKVILLE SHELBY CO	SHELBY CO MOBILE COLORED SCHOOL	N	✓	✓	✓		
OBERLES SHELBY CO	SHELBY CO MOBILE OBERLES STORE	N	✓	✓	✓		
OOLTEWAH HAMILTON CO	HEALTH CENTER	ALL	✓	✓	✓		
PARIS HENRY CO	CO HEALTH DEPT	ALL	✓	✓	✓		
PARSONS DECATUR CO	COUNTY HEALTH OEPT	ALL	✓	✓	✓		
PEAKS BELLS SHELBY CO	CO MOBILE UNIT PEAKS STORE	N	✓	✓	✓		
PELHAM GRUNDY CO	COUNTY HEALTH DEPT	ALL	✓	✓	✓		
PESTHOUSE SHELBY CO	CO MOBILE UNIT CO PESTHOUSE	N	✓	✓	✓		
PIKEVILLE BLEDSOE CO	CITY CLINIC	ALL	✓	✓	✓		

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TENNESSEE

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
PORTERS SHELBY CO	SHELBY CO MOBILE PORTERS STORE	N	✓	✓	✓		
PORTLAND SUMNER CO	COUNTY HEALTH DEPT WILKINSON WISEMAN UN	ALL	✓	✓	✓		
PULASKI GILES CO	V D CLINIC EAST MADISON ST	ALL	✓	✓	✓		
RALEIGH SHELBY CO	SHELBY CO MOBILE GOROONS STORE	ALL	✓	✓	✓		
RIDGELY LAKE CO	V D CLINIC LOGCABIN W REO LIGHT	ALL	✓	✓	✓		
RIGGINS SHELBY CO	SHELBY CO MOBILE RIGGINS STORE	N	✓	✓	✓		
RIPLEY LAUDERDALE CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
ROCKWOOD ROANE CO	COUNTY HEALTH DEPT CHAMBERLAIN MEM HOSP	ALL	✓		✓		
ROGERSVILLE HAWKINS CO	COUNTY CLINIC	ALL	✓	✓	✓		
ROSSVILLE FAYETTE CO	COUNTY CLINIC WALLER BLDG	ALL	✓	✓	✓		
SALTILLO HARDIN CO	COUNTY CLINIC	ALL	✓	✓	✓		
SANDERLINS SHELBY CO	CO MOBILE UNIT SANDERLINS GROCERY	N	✓	✓	✓		
SAVANNAH HARDIN CO	COUNTY CLINIC	ALL	✓	✓	✓		
SEVIERVILLE SEVIER CO	COUNTY HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
SHARON WEAKLEY CO	CITY CLINIC SHAHON BANK BLDG	ALL	✓	✓	✓		
SHELBYVILLE BEDFORD CO	V D CLINIC COUNTY HOSPITAL	ALL	✓	✓	✓		
SMYRNA RUTHERFORD CO	COUNTY V D CLINIC MT ZION BAPT CHURCH	ALL	✓	✓	✓		
SOODY HAMILTON CO	HEALTH CENTER GRAMMER SCHOOL	ALL	✓	✓	✓		
SOMERVILLE FAYETTE CO	V D CLINIC	ALL	✓	✓	✓		
SPRINGHILL CHURCH SHELBY CO	SHELBY CO MOBILE SPRING HILL CHURCH	N	✓	✓	✓		
SUMMIT HAMILTON CO	HEALTH CENTER	ALL	✓	✓	✓		
SWEETWATER MONROE CO	COUNTY HEALTH DEPT 118 MORRIS ST	ALL	✓	✓	✓		
TIPTONVILLE LAKE CO	V D CLINIC COURT HOUSE	ALL	✓	✓	✓		
TRACY CITY GRUNDY CO	COUNTY CLINIC	ALL	✓	✓	✓		
TRENTON GIBSON CO	COUNTY HEALTH DEPT 200 EATON ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
TULLAHOMA COFFEE CO	V O CLINIC HEALTH OEPT	ALL	✓	✓	✓		
TULLY STATION SHELBY CO	SHELBY CO MOBILE TULLYS STORE	N	✓	✓	✓		
UNION CITY OBION CO	COUNTY HEALTH OEPT THIRO AND CHURCH STS	ALL	✓	✓	✓		
WARTBURG MORGAN CO	COUNTY CLINIC COURTHOUSE SQUARE	ALL	✓	✓	✓		
WAVERLY HUMPHREYS CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
WEAVER SHELBY CO	SHELBY CO MOBILE WEAVER SCHOOL	N	✓	✓	✓		
WEST JUNCTION SHELBY CO	SHELBY CO MOBILE MARTINS STORE	N	✓	✓	✓		
WESTMORELANO SUMNER CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
WHITE STATION SHELBY CO	SHELBY CO MOBILE SCOTTS GROCERY	N	✓	✓	✓		
WINCHESTER FRANKLIN CO	COUNTY HEALTH OEPT 8TH AVENUE	ALL	✓	✓	✓		
WOOOSTOCK SHELBY CO	SHELBY CO MOBILE STORE	N	✓	✓	✓		
	TEXAS						
ABILENE TAYLOR CO	ABILENE TAYLOR CLIN COURTHOUSE	ALL	✓	✓	✓		
ARLINGTON TARRANT CO	COUNTY V D CLINIC CITY HALL	ALL	✓	✓	✓		
ATLANTA CASS CO	COUNTY CLINIC	ALL	✓	✓	✓		
AUSTIN TRAVIS CO	AUSTIN TRAVIS CLINIC BRECKENRIOGE HOSP	ALL	✓	✓	✓		
BAY CITY MATAGORDA CO	V O CLINIC COUNTY HOSPITAL	ALL	✓	✓	✓		
BEAUMONT JEFFERSON CO	V O CLINIC 855 TRINITY ST	ALL	✓	✓	✓		
BEEVILLE BEE CO	COUNTY CLINIC	ALL	✓	✓	✓		
BESSMAY JASPER CO	CITY CLINIC	ALL	✓	✓	✓		
BIG SPRING HOWARD CO	CITY CLINIC V D CLINIC BLDG	ALL	✓	✓	✓		
BOSTON BOWIE CO	COUNTY V O CLINIC COUNTY JAIL	ALL	✓	✓	✓		
BROWNFIELO TERRY CO	V O CLINIC CLINIC BUILOING	ALL	✓	✓	✓		

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TEXAS

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
BROWNSVILLE CAMERON CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
BROWNWOOD BROWN CO	CITY COUNTY CLINIC AMERICAN LEGION BLDG	ALL	✓	✓	✓		
BRYAN BRAZOS CO	BRAZOS BRYAN CLINIC CITY HALL	ALL	✓	✓	✓		
CALL NEWTON CO	V D CLINIC MEDICAL QUARTERS	ALL	✓	✓	✓		
CAMERON MILAM CO	COUNTY HEALTH UNIT	ALL	✓	✓	✓		
CANUTILLO EL PASO CO	CITY CLINIC HEALTH DEPT BLDG	ALL	✓	✓	✓		
CLINT EL PASO CO	CITY CLINIC HEALTH DEPT BLDG	ALL	✓	✓	✓		
COLEMAN COLEMAN CO	COUNTY CLINIC OVERALL HOSPITAL	ALL	✓	✓	✓		
COMMERCE HUNT CO	V D CLINIC CLINIC BLDG	ALL	✓	✓	✓		
COOPER DELTA CO	COUNTY CLINIC JANES HOSPITAL	ALL	✓	✓	✓		
CORPUS CHRISTI NUECES CO	CITY CLINIC CLINIC BLDG	ALL	✓	✓	✓		
CORSICANA NAVARRO CO	COUNTY V U CLINIC	ALL	✓	✓	✓		
CROCKETT HOUSTON CO	COUNTY V D CLINIC V D BLDG	ALL	✓	✓	✓		
CRYSTAL CITY ZAVALO CO	V D CLINIC HEALTH UNIT QUARTERS	ALL	✓	✓	✓		
DALLAS DALLAS CO	DALLAS V D CLINIC PARKLAND HOSPITAL	ALL	✓	✓	✓		
DALLAS DALLAS CO	R F MEMORIAL CLINIC 3617 MAPLE AVE	ALL	✓	✓	✓		
DE KALB BOWIE CO	CITY CLINIC OLD FEDERAL BLDG	ALL	✓	✓	✓		
DEL RIO VAL VERDE CO	CITY CLINIC MAIN ST	ALL	✓	✓	✓		
DEWEYVILLE NEWTON CO	V D CLINIC MEDICAL QUARTERS	ALL	✓	✓	✓		
EDINBURG HIDALGO CO	COUNTY CLINIC	ALL	✓	✓	✓		
EL PASO EL PASO CO	COUNTY CLINIC NO 1 COURT HOUSE	ALL	✓	✓	✓		
FABENS EL PASO CO	CITY CLINIC	ALL	✓	✓	✓		
FORT WORTH TARRANT CO	CITY CLINIC 315 EAST 5TH ST	ALL	✓	✓	✓		
GAINESVILLE COOKE CO	CITY CLINIC COURTHOUSE	ALL	✓	✓	✓		
GALVESTON GALVESTON CO	JOHN SEALY HOSPITAL UNIVERSITY OF TEXAS	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
GREENVILLE HUNT CO	CITY CLINIC COURTHOUSE	ALL	✓	✓	✓		
HARLINGEN CAMERON CO	CITY CLINIC CITY HALL	ALL	✓	✓	✓		
HEARNE ROBERTSON CO	COUNTY V D CLINIC HEALTH UNIT BLDG	ALL	✓	✓	✓		
HILLSBORO HILL CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
HOUSTON HARRIS CO	CITY CLINIC NO 1 OLD JEFF DAVIS HOSP	ALL	✓	✓	✓		
HOUSTON HARRIS CO	CITY V D CLINIC NO 2 HEALTH CENTER NO 2	ALL	✓	✓	✓		
HOUSTON HARRIS CO	CITY V D CLINIC NO 3 HEALTH CENTER NO 3	ALL	✓	✓	✓		
JASPER JASPER CO	JASPER NEWTON CLINIC HEALTH UNIT BLDG	ALL	✓	✓	✓		
KIRBYVILLE JASPER CO	V D CLINIC HIGH SCHOOL BLDG	ALL	✓	✓	✓		
KOUNTZ HARDIN CO	CITY CLINIC COUNTY NURSES OFFICE	ALL	✓	✓	✓		
LAMESA DAWSON CO	V D CLINIC HEALTH UNIT BLDG	ALL	✓	✓	✓		
LAREDO WEBB CO	CITY CLINIC CITY HALL ANNEX	ALL	✓	✓	✓		
LIBERTY CHAMBERS CO	CITY CO HEALTH UNIT BOX 71	ALL	✓	✓	✓		
LINDEN CASS CO	COUNTY V D CLINIC CITY HALL ANNEX	ALL	✓	✓	✓		
LONGVIEW GREGG CO	CITY CLINIC HEALTH DEPT BLDG	ALL	✓	✓	✓		
MC ALLEN HIDALGO CO	CITY CLINIC CLINIC BLDG MAIN ST	ALL	✓	✓	✓		
MC KINNEY COLLIN CO	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
MANSFIELD TARRANT CO	COUNTY V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
MAUD BOWIE CO	CITY CLINIC	ALL	✓	✓	✓		
MIDLAND MIDLAND CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
MINERAL WELLS PALO PINTO CO	V D CLINIC NAZARETH HOSPITAL	ALL	✓	✓	✓		
NEW BOSTON BOWIE CO	CITY CLINIC	ALL	✓	✓	✓		
NEWTON NEWTON CO	CITY CLINIC	ALL	✓	✓	✓		
ODESSA ECTOR CO	COUNTY CLINIC	ALL	✓	✓	✓		
PALACIOS MATAGORDA CO	V D CLINIC HEALTH UNIT OFFICES	ALL	✓	✓	✓		

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TEXAS

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
PAMPA GRAY CO	CITY CLINIC CITY HALL	ALL	✓	✓	✓		
PORT ARTHUR JEFFERSON CO	CITY CLINIC CITY HALL	ALL	✓	✓	✓		
PORT ISABEL CAMERON CO	CITY CLINIC DR HOCKADAYS OFFICE	ALL	✓	✓	✓		
PORT LAVACO CALHOUN CO	COUNTY V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
RAYMONDVILLE WILLACY CO	COUNTY CLINIC CLINIC BLD DR CONLEY	ALL	✓	✓	✓		
ROBSTOWN NUECES CO	COUNTY V D CLINIC FIRE STATION BLDG	ALL	✓	✓	✓		
SABINAL UVALOE CO	CITY CLINIC	ALL	✓	✓	✓		
SAN ANGELO TOM GREEN CO	CITY CLINIC CITY HALL	ALL	✓	✓	✓		
SAN ANTONIO BEXAR CO	CITY CLINIC 102 DWYER AVE	ALL	✓	✓	✓		
SAN AUGUSTINE SAN AUGUSTINE CO	CITY CLINIC COURTHOUSE	ALL	✓	✓	✓		
SAN BENITO CAMERON CO	CITY CLINIC HEALTH UNIT BLDG	ALL	✓	✓	✓		
SAN ELIZARIO EL PASO CO	CITY CLINIC	ALL	✓	✓	✓		
SHAMROCK WHEELER CO	CITY CLINIC	ALL	✓	✓	✓		
SOCORRO EL PASO CO	CITY CLINIC	ALL	✓	✓	✓		
TEAGUE FREESTONE CO	CITY COUNTY CLINIC CITY HOSPITAL	ALL	✓	✓	✓		
TEXARKANA BOWIE CO	CITY CLINIC OLD FEDERAL BLDG	ALL	✓	✓	✓		
TYLER SMITH CO	TYLER SMITH CLINIC COURTHOUSE	ALL	✓	✓	✓		
UVALOE UVALDE CO	COUNTY CLINIC HEALTH CENTER BLDG	ALL	✓	✓	✓		
VICTORIA VICTORIA CO	CITY COUNTY CLINIC 2ND FLOOR WOODS BLDG	ALL	✓	✓	✓		
WACO MCLENNAN CO	V D CLINIC CITY HOSPITAL	ALL	✓	✓	✓		
WAXAHACHIE ELLIS CO	CITY CLINIC 200 NORTH JACKSON ST	ALL	✓	✓	✓		
WEATHERFORD PARKER CO	V D CLINIC HEALTH UNIT BLDG	ALL	✓	✓	✓		
WESLACO HIDALGO CO	CITY CLINIC	ALL	✓	✓	✓		
WHARTON WHARTON CO	COUNTY V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
WHEELER WHEELER CO	COUNTY CLINIC WHEELER HOSPITAL	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
WICHITA FALLS WICHITA CO	CITY CLINIC CITY AUDITORIUM	ALL	✓	✓	✓		
WIERGATE NEWTON CO	V D CLINIC MEDICAL QUARTERS	ALL	✓	✓	✓		
WOODVILLE TYLER CO	HARDIN TYLER CLINIC COURTHOUSE	ALL	✓	✓	✓		
YSLETA EL PASO CO	V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
	UTAH						
OGDEN WEBER CO	CITY CLINIC CITY AND COUNTY BLDG	ALL	✓	✓	✓		
SALT LAKE CITY SALT LAKE CO	COUNTY CLINIC 21ST S AND STATE STS	ALL	✓	✓	✓		
SALT LAKE CITY SALT LAKE CO	CITY COUNTY CLINIC 115 SO STATE ST	ALL	✓	✓	✓		
	VERMONT **						
BURLINGTON CHITTENDEN CO	FREE DISPENSARY U OF VT MEDICAL SCH	ALL	✓	✓	✓		
	VIRGINIA						
ABINGDON WASHINGTON CO	CITY CLINIC CO HEALTH DEPT	ALL	✓	✓	✓		
ALEXANDRIA	COMMUNITY H CENTER 218 SO COLUMBUS ST	ALL	✓	✓		✓	
ALEXANDRIA	WOODLAWN CLINIC CLINIC BLDG R F D 1	ALL	✓	✓	✓		
ALTAVISTA CAMPBELL CO	CITY CLINIC MUNICIPAL BUILDING	ALL	✓		✓		
ALTON HALIFAX CO	CITY CLINIC	ALL	✓	✓	✓		
AMHERST AMHERST CO	COUNTY CLINIC	ALL	✓	✓	✓		
APPALACHIA WISE CO	V D CLINIC	ALL	✓		✓		
ARLINGTON ARLINGTON CO	CLARENDON CLINIC 1119 NO HUDSON ST	ALL	✓		✓		

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** IN ADDITION TO CLINICS LISTED, THE ADDRESSES OF PHYSICIANS GIVING TREATMENT FOR VENEREAL DISEASES UNDER THE STATE PLAN MAY BE OBTAINED FROM STATE, COUNTY, AND MUNICIPAL OFFICERS.

VIRGINIA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
ARVONIA BUCKINGHAM CO	CITY CLINIC	ALL	✓	✓	✓		
ASHLAND HANOVER CO	V U CLINIC HEALTH DEPT	ALL	✓	✓	✓		
BEAVER DAM HANOVER CO	MONTPELIER CLINIC	ALL	✓	✓	✓		
BEDFORD BEDFORD CO	V U CLINIC MUNICIPAL BLUG	ALL	✓	✓	✓		
BERRYVILLE CLARKE CO	CITY CLINIC	ALL	✓		✓		
BLACKSTONE NOTTOWAY CO	CITY CLINIC POWER BUILDING	ALL	✓	✓	✓		
BLAIRS PITTSYLVANIA CO	TAYLORSVILLE CLINIC ROUTE NO 1	ALL	✓	✓	✓		
BLUEFIELD TAZEWELL CO	CITY CLINIC	ALL	✓		✓		
BOYKINS SOUTHAMPTON CO	V U CLINIC HEALTH CENTER	ALL	✓	✓	✓		
BRISTOL WASHINGTON CO	CITY CLINIC KINGS MT MEM HOSP	ALL	✓	✓	✓		
BUCKINGHAM BUCKINGHAM CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
BURKEVILLE NOTTOWAY CO	CITY CLINIC MUNICIPAL BUILDING	ALL	✓	✓	✓		
CAPE CHARLES NORTHAMPTON CO	CITY CLINIC TIMES BUILUING	ALL	✓		✓		
CHARLOTTE C H CHARLOTTE CO	COUNTY CLINIC	ALL	✓		✓		
CHARLOTTESVILLE ALBENARLE CO	CITY CLINIC CITY HALL	ALL	✓	✓	✓		
CHARLOTTESVILLE ALBEMARLE CO	V U CLINIC U OF VIRGINIA HOSP	ALL	✓	✓	✓		
CHASE CITY MECKLENBURG CO	CITY CLINIC UEPT STORE BLDG	ALL	✓		✓		
CHATHAM PITTSYLVANIA CO	CITY CLINIC COUNTY COURTHOUSE	ALL	✓	✓	✓		
CHESTERFIELD CHESTERFIELD CO	UUTCH GAP V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
CHRISTIANBURG MONTCOMERY CO	V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
CLARKSVILLE MECKLENBURG CO	CITY CLINIC HEALTH UEPT	ALL	✓		✓		
CLIFTON FORGE ALLEGHENY CO	V D CLINIC COURTHOUSE ANNEX	ALL	✓	✓	✓		
COVINGTON ALLEGHENY CO	CITY CLINIC	ALL	✓		✓		
CUMBERLAND CUMBERLAND CO	COUNTY CLINIC	ALL	✓	✓	✓		
DANVILLE PITTSYLVANIA CO	HEALTH DEPT CLINIC	ALL	✓		✓		

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
DENBIGH WARWICK CO	CITY CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
DISPUTANTA PRINCE GEORGE CO	TOWN CLINIC HEALTH CENTER	ALL	✓	✓	✓		
DRIVERS NANSEMOND CO	CITY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
DUBLIN PULASKI CO	HEALTH CENTER MUNICIPAL BLDG	ALL	✓	✓	✓		
EASTVILLE NORTHAMPTON CO	CITY CLINIC COURTHOUSE	ALL	✓		✓		
ELLERSON HANOVER CO	CITY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
EMPORIA GREENVILLE CO	V D CLINIC COURTHOUSE	N	✓	✓	✓		
EMPORIA GREENSVILLE CO	V D CLINIC MASONIC BUILDING	W	✓	✓	✓		
FAIRFAX FAIRFAX CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
FALLS CHURCH FAIRFAX CO	CITY CLINIC ODD FELLOWS HALL	ALL	✓	✓	✓		
FARMVILLE PRINCE EDWARD CO	CITY CLINIC SOUTHSIDE COM HOSP	ALL	✓	✓			✓
FINCASTLE BOTETOURT CO	CITY CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
FRANKLIN SOUTHAMPTON CO	V D CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
FREDERICKSBURG SPOTSYLVANIA CO	CITY CLINIC MUNICIPAL BLDG	ALL	✓	✓		✓	
FRONT ROYAL WARREN CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
GORDONSVILLE ORANGE CO	V D CLINIC YOWELL GROCERY STORE	ALL	✓	✓	✓		
GRETNA PITTSYLVANIA CO	V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
GRUNDY BUCHANAN CO	CITY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
HAMPTON ELIZABETH CITY CO	V D CLINIC DIXIE HOSPITAL	ALL	✓	✓	✓		
HARRISONBURG ROCKINGHAM CO	V D CLINIC 234 EAST MARKET ST	ALL	✓	✓	✓		
HOPEWELL PRINCE GEORGE CO	CITY HEALTH DEPT 200 NORTH 9TH ST	ALL	✓	✓		✓	
HURLEY BUCHANAN CO	CITY CLINIC	ALL	✓	✓	✓		
LAWRENCEVILLE BRUNSWICK CO	V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
LEBANON RUSSELL CO	CITY CLINIC	ALL	✓	✓	✓		
LEXINGTON ROCKBRIDGE CO	V D CLINIC JACKSON MEM HOSP	ALL	✓	✓	✓		

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VIRGINIA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
LURAY PAGE CO	V O CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
LYNCHBURG CAMPBELL CO	V O CLINIC 10TH AND CHURCH STS	ALL	✓	✓	✓		
MADISON HEIGHTS AMHERST CO	CITY CLINIC	ALL	✓	✓	✓		
MANASSAS PRINCE WILLIAM CO	CITY CLINIC HEALTH DEPT	ALL	✓	✓	✓		
MARION SMYTH CO	V O CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
MARTINSVILLE HENRY CO	COUNTY V D CLINIC	ALL	✓	✓		✓	
MATHEWS MATHEWS CO	COUNTY V O CLINIC	ALL	✓	✓		✓	
MIDDLEBURG LOUDOUN CO	HEALTH CENTER MADISON ST	ALL	✓	✓		✓	
NASSAWADOX NORTHAMPTON CO	CITY CLINIC MEMORIAL HOSPITAL	ALL	✓	✓	✓		
NEWPORT NEWS WARWICK CO	V O CLINIC 2516 WASHINGTON ST	ALL	✓	✓	✓		
NEWPORT NEWS WARWICK CO	WHITTAKER HOSP OPD 1014 29TH ST	ALL	✓	✓	✓		
NORFOLK NORFOLK CO	CO MED SOC CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
NORFOLK NORFOLK CO	KINGS DAUGHTERS CLIN 300 WEST YORK STREET	C	✓	✓	✓		
NORFOLK NORFOLK CO	PUBLIC CLINIC 449 EAST BUTE ST	N	✓	✓	✓	✓	
NORTON WISE CO	CITY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
ORANGE ORANGE CO	COUNTY V O CLINIC MAIN ST	ALL	✓	✓	✓		
PETERSBURG DINWIDDIE CO	HEALTH CENTER 14 16 NO MARKET ST	ALL	✓	✓		✓	✓
PORTSMOUTH NORFOLK CO	CITY HEALTH DEPT NEW MARKET BUILDING	ALL	✓	✓	✓		
PORTSMOUTH NORFOLK CO	PUBLIC V D CLINIC 401 SOUTH GREEN ST	ALL	✓		✓	✓	
PRINCESS ANNE PRINCESS ANNE CO	COUNTY V D CLINIC COURTHOUSE	ALL	✓		✓		
PULASKI PULASKI CO	COUNTY V D CLINIC 93 SECOND ST N W	ALL	✓	✓	✓		
RADFORD MONTGOMERY CO	V O CLINIC HEALTH CENTER	ALL	✓	✓	✓		
RICHLANDS TAZEWELL CO	CITY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
RICHMOND HENRICO CO	CH HILL V D CLINIC 605 NORTH 24TH ST	ALL	✓	✓	✓		
RICHMOND HENRICO CO	COMMUNITY CLINIC 2 WEST MARSHALL ST	ALL	✓	✓	✓	✓	

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
RICHMOND HENRICO CO	VA MED COLL CLINIC 1201 E MARSHALL ST	ALL	✓	✓		✓	
RICHMOND HENRICO CO	WEST CARY CLINIC 1106 A WEST CARY ST	ALL	✓	✓	✓		
ROANOKE ROANOKE CO	V D CLINIC 209 CHURCH AVE S W	ALL	✓	✓	✓		
ST PAUL WISE CO	CITY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
SALEM ROANOKE CO	COMMUNITY V D CLINIC 9 COLLEGE AVE	ALL	✓	✓	✓		
SOUTH BOSTON HALIFAX CO	V D CLINIC COUNTY HEALTH DEPT	ALL	✓	✓	✓		
SOUTH HILL MECKLENBURG CO	V D CLINIC OLD MASONIC HALL	ALL	✓	✓		✓	
STAUNTON AUGUSTA CO	V D CLINIC 10 EAST JOHNSON ST	ALL	✓	✓	✓		
STONY CREEK SUSSEX CO	CITY CLINIC HEALTH OFFICE BLDG	ALL	✓	✓	✓		
SUFFOLK NANSEMOND CO	CITY CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
TAPPAHANNOCK ESSEX CO	COUNTY CLINIC	ALL	✓			✓	
TOANO JAMES CITY CO	V D CLINIC HEALTH DEPARTMENT	ALL	✓		✓		
TOWNSEND NORTHAMPTON CO	V D CLINIC BANK BUILDING	ALL	✓	✓	✓		
URBANNA MIDDLESEX CO	COUNTY CLINIC HEALTH CENTER	ALL	✓		✓		
VINTON ROANOKE CO	COMMUNITY WELFARE MUNICIPAL BUILDING	ALL	✓	✓	✓		
VIRGINIA BEACH PRINCESS ANNE CO	CITY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
WAKEFIELD SUSSEX CO	CITY CLINIC TOWN HALL	ALL	✓	✓	✓		
WAVERLY SUSSEX CO	CITY CLINIC MAIN ST	ALL	✓	✓	✓		
WAYNESBORO AUGUSTA CO	V D CLINIC CITY HALL ANNEX	ALL	✓	✓	✓		
WILLIAMSBURG JAMES CITY CO	V D CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
WOODSTOCK SHENANDOAH CO	V D CLINIC HEALTH OFFICE	ALL	✓	✓	✓		
WYTHEVILLE WYTHE CO	V D CLINIC MAIN ST	ALL	✓		✓		
YORKTOWN YORK CO	CITY CLINIC	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
	WASHINGTON						
ABERDEEN GRAYS HARBOR CO	CO PUBLIC HEALTH CL CITY GENERAL HOSP	ALL	✓	✓	✓		
BELLINGHAM WHATCOM CO	CO PUBLIC HEALTH CL COURTHOUSE G STREET	ALL	✓	✓	✓		
BREMERTON KITSAP CO	CO H O CLINIC FARRAGUT ST	ALL	✓	✓	✓		
CENTRALIA LEWIS CO	CO H O CLINIC COUNTY HOSPITAL	ALL	✓	✓	✓		
CENTRALIA LEWIS CO	V O CLINIC DR KROGERS OFFICE	ALL	✓	✓	✓		
COLFAX WHITMAN CO	COUNTY HEALTH DEPT GRADY BLDG	ALL	✓	✓	✓		
EVERETT SNOHOMISH CO	COUNTY HEALTH DEPT COUNTY BUILDING	ALL	✓	✓	✓		
KELSO COWLITZ CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
OLYMPIA THURSTON CO	COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
PORT ANGELES CLALLAM CO	CITY CO HEALTH DEPT COURTHOUSE	ALL	✓	✓	✓		
SEATTLE KING CO	CITY CLINIC PUBLIC SAFETY BLDG	ALL	✓	✓	✓		
SEATTLE KING CO	HEALTH DEPT CLINIC 416 YESLER WAY	ALL	✓	✓	✓	✓	
SEATTLE KING CO	COUNTY CLINIC 325 9TH AVE	ALL	✓	✓	✓		
SPOKANE SPOKANE CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
TACOMA PIERCE CO	TACOMA P H CLINIC 322 PROVIDENT BLDG	ALL	✓	✓	✓	✓	
VANCOUVER CLARK CO	COUNTY HEALTH DEPT MUNICIPAL BLDG	ALL	✓	✓	✓		
WALLA WALLA WALLA WALLA CO	CITY COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
WENATCHEE CHELAN CO	COUNTY CLINIC COURTHOUSE BLDG	ALL	✓	✓	✓		
YAKIMA YAKIMA CO	COUNTY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
	WEST VIRGINIA						
BECKLEY RALEIGH CO	COUNTY V O CLINIC COURTHOUSE	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
BLUEFIELD MERCER CO	CITY V D CLINIC MUNICIPAL BUILDING	ALL	✓	✓	✓		
BUCKHANNON UPSHUR CO	COUNTY V D CLINIC OLD BANK BLDG	ALL	✓	✓	✓		
CHARLESTON KANAWHA CO	CITY V D CLINIC CITY BUILDING	ALL	✓	✓	✓		
CHARLESTON KANAWHA CO	COUNTY V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
CHARLES TOWN JEFFERSON CO	COUNTY V D CLINIC	ALL	✓	✓	✓		
CLARKSBURG HARRISON CO	CITY COUNTY CLINIC COURTHOUSE	ALL	✓	✓	✓		
CLAY CLAY CO	COUNTY V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
EAST RAINELLE GREENBRIER CO	COUNTY V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
ELK GARDEN MINERAL	COUNTY V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
ELKINS RANDOLPH CO	COUNTY V D CLINIC PUB ASSIST BLDG	ALL	✓	✓	✓		
FAIRMONT MARION CO	COUNTY V D CLINIC CITY BLDG	ALL	✓	✓	✓		
FARMINGTON MARION CO	COUNTY V D CLINIC	ALL	✓	✓	✓		
FAYETTEVILLE FAYETTE CO	COUNTY V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
GLENVILLE GILMER CO	COUNTY V D CLINIC CHURCH STREET	ALL	✓	✓	✓		
GRAFTON TAYLOR CO	COUNTY V D CLINIC CITY HOSPITAL	ALL	✓	✓	✓		
GRANTSVILLE CALHOUN CO	COUNTY V D CLINIC HEALTH CENTER	ALL	✓	✓	✓		
HAMLIN LINCOLN CO	COUNTY V D CLINIC PUB ASSIST BLDG	ALL	✓	✓	✓		
HARRISVILLE RITCHIE CO	COUNTY V D CLINIC MORRIS BLDG	ALL	✓	✓	✓		
HINTON SUMMERS CO	COUNTY V D CLINIC DR J W STOKES OFFICE	ALL	✓	✓	✓		
HUNTINGTON CABELL CO	CITY V D CLINIC CITY BUILDING	ALL	✓	✓	✓	✓	
KEYSER MINERAL CO	COUNTY V D CLINIC COURTHOUSE	ALL	✓	✓	✓		
KINGWOOD PRESTON CO	COUNTY V D CLINIC	ALL	✓	✓	✓		
LEWISBURG GREENBRIER CO	COUNTY V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
LOGAN LOGAN CO	COUNTY CLINIC COURTHOUSE BASEMENT	ALL	✓	✓	✓		
MADISON BOONE CO	COUNTY V D CLINIC COURTHOUSE	ALL	✓	✓	✓		

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WEST VIRGINIA

CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
MAN LOGAN CO	V O CLINIC PIGGLY WIGGLY BLDG	ALL	✓	✓	✓		
MARLINTON POCAHONTAS CO	COUNTY V O CLINIC COUNTY NURSES OFFICE	ALL	✓	✓	✓		
MARTINSBURG BERKELEY CO	COUNTY V O CLINIC COUNTY COURTHOUSE	ALL	✓	✓	✓		
MONTGOMERY FAYETTE CO	COUNTY V O CLINIC 6 ST AND BRIDGE AVE	ALL	✓	✓	✓		
MORGANTOWN MONONGALIA CO	COUNTY V O CLINIC 227 KIRK ST	ALL	✓	✓	✓		
MOUNDSVILLE MARSHALL CO	COUNTY V O CLINIC 315 JEFFERSON AVE	ALL	✓	✓	✓		
MULLENS WYOMING CO	COUNTY V O CLINIC CO HEALTH DEPT	ALL	✓	✓	✓		
NEW CUMBERLAND HANCOCK CO	COUNTY V O CLINIC CO HEALTH DEPT	ALL	✓	✓	✓		
NEW MARTINSVILLE WETZEL CO	COUNTY V O CLINIC CO HEALTH DEPT	ALL	✓	✓	✓		
OMAR LOGAN CO	COUNTY V O CLINIC W VA COALCOKE BLDG	ALL	✓	✓	✓		
PARKERSBURG WOOD CO	COUNTY V O CLINIC CITY BUILDING ANNEX	ALL	✓	✓	✓		
PARSONS TUCKER CO	COUNTY V O CLINIC SECOND STREET	ALL	✓	✓	✓		
PETERSBURG GRANT CO	COUNTY V O CLINIC NEAR COURTHOUSE	ALL	✓	✓	✓		
PHILIPPI BARBOUR CO	COUNTY V O CLINIC FIRST NATL BANK BLDG	ALL	✓	✓	✓		
POINT PLEASANT MASON CO	COUNTY V O CLINIC CO HEALTH DEPT	ALL	✓	✓	✓		
PRINCETON MERCER CO	COUNTY V O CLINIC COURTHOUSE	ALL	✓	✓	✓		
RICHWOOD NICHOLAS CO	COUNTY V O CLINIC OAKFORD AND MAIN STS	ALL	✓	✓	✓		
RIPLEY JACKSON CO	COUNTY V O CLINIC HEALTH DEPT	ALL	✓	✓	✓		
ROMNEY HAMPSHIRE CO	COUNTY V D CLINIC SHEAR BLDG	ALL	✓	✓	✓		
SHEPHERDSTOWN JEFFERSON CO	COUNTY V D CLINIC FIREMANS HALL	ALL	✓	✓	✓		
SPENCER ROANE CO	COUNTY V D CLINIC BELL TELEPHONE BLDG	ALL	✓	✓	✓		
SUMMERSVILLE NICHOLAS CO	COUNTY V D CLINIC ST NICHOLAS HOTEL	ALL	✓	✓	✓		
SUTTON BRAXTON CO	COUNTY V D CLINIC BRIDGE STREET	ALL	✓	✓	✓		
UNION MONROE CO	COUNTY CLINIC CALDWELL BLDG	ALL	✓	✓	✓		
WAYNE WAYNE CO	COUNTY V O CLINIC COURTHOUSE	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
WEBSTER SPRINGS WEBSTER CO	COUNTY V D CLINIC CO HEALTH DEPT	ALL	✓	✓	✓		
WEIRTON HANCOCK CO	COUNTY V D CLINIC CHRISTIAN CENTER	ALL	✓	✓	✓		
WELCH MCDOWELL CO	COUNTY V D CLINIC EMERGENCY HOSP	ALL	✓	✓	✓		
WELLSBURG BROOKE CO	COUNTY V D CLINIC NATL BANK BLDG	ALL	✓	✓	✓		
WESTON LEWIS CO	V D CLINIC CO HEALTH DEPT	ALL	✓	✓	✓		
WEST UNION DODDRIDGE CO	COUNTY V D CLINIC COLUMBUS STREET	ALL	✓	✓	✓		
WHEELING OHIO CO	CITY CO V D CLINIC OHIO VALLEY GEN HOSP	ALL	✓	✓	✓		
WHITESVILLE BOONE CO	COUNTY V D CLINIC HEALTH DEPT	ALL	✓	✓	✓		
WILLIAMSON MINGO CO	COUNTY V D CLINIC MEMORIAL BLDG	ALL	✓	✓	✓		
WINFIELD PUTNAM CO	COUNTY V D CLINIC COURTHOUSE ANNEX	ALL	✓	✓	✓		
	WISCONSIN						
BELOIT ROCK CO	CITY HEALTH CLINIC CITY HEALTH DEPT	ALL	✓	✓	✓		
GREEN BAY BROWN CO	CITY HEALTH CLINIC 523 HOWE ST	ALL	✓	✓	✓		
JANESVILLE ROCK CO	STATE CLINIC CITY HALL	ALL	✓	✓	✓		
KENOSHA KENOSHA CO	STATE CLINIC CITY HALL	ALL	✓	✓	✓		
LA CROSSE LA CROSSE CO	STATE CLINIC CITY HALL	ALL	✓	✓	✓		
MADISON DANE CO	STATE CLINIC 112 NO HAMILTONST	ALL	✓	✓	✓		
MILWAUKEE MILWAUKEE CO	CITY HEALTH DEPT CITY HALL	ALL	✓	✓	✓		
MILWAUKEE MILWAUKEE CO	COUNTY DISPENSARY 2430 W WISCONSIN AVE	ALL	✓		✓		
MILWAUKEE MILWAUKEE CO	MT SINAI CLINIC 908 NO TWELFTH ST	ALL	✓	✓		✓	
MILWAUKEE MILWAUKEE CO	NIGHT CLINIC CITY HALL	ALL	✓		✓		
MILWAUKEE MILWAUKEE CO	V D CLINIC 904 WEST VINE ST	N	✓	✓	✓		
OSHKOSH WINNEBAGO CO	STATE CLINIC 28 STATE ST	ALL	✓	✓	✓		

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CITY AND COUNTY	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
RACINE RACINE CO	CITY HEALTH CLINIC CITY HALL	ALL	✓	✓	✓		
SUPERIOR DOUGLAS CO	STATE CLINIC 1323 BROADWAY	ALL	✓	✓	✓		
WAUKESHA WAUKESHA CO	STATE CLINIC WAUKESHA MEM HOSP	ALL	✓		✓		
WAUSAU MARATHON CO	STATE CLINIC 314 SCOTT ST	ALL	✓	✓	✓		
	WYOMING						
CASPER NATRONA CO	CITY CLINIC CO HEALTH UNIT BLDG	ALL	✓	✓	✓		
CHEYENNE LARAMIE CO	CITY CLINIC MEMORIAL HOSPITAL	ALL	✓	✓	✓		
LARAMIE ALBANY CO	CITY CLINIC SIMPSON BLDG	ALL	✓	✓	✓		
ROCK SPRINGS SWEETWATER CO	CITY CLINIC GENERAL HOSPITAL	ALL	✓	✓	✓		

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Directory of

VENEREAL DISEASE CLINICS FOR FOREIGN SEAMEN

UNITED STATES PUBLIC HEALTH SERVICE
Supplement No. 4-A to Venereal Disease Information
1943

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FEDERAL SECURITY AGENCY

PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

United States
Government Printing Office
Washington : 1943

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Preface to:

Venereal Disease Clinic Directory for Foreign Seamen

If you know or suspect that you have syphilis or gonorrhea, call at the clinic listed in this book which is most convenient when next you have shore leave. Failure to take treatment now may lead to blindness, insanity, heart disease, sterility, or other serious and painful results.

Your seaman's card will identify you at any of the clinics or hospitals listed. These clinics serve you at the request of the United States Public Health Service.

Se o Sr. pensa ou sabe que tem sífilis (lúes) ou blenorragia (gonorréia), visite a clínica inscrita neste libreto e que lhe seja mais conveniente na próxima vez que descer à terra. Caso não fizer tratamento agora, V. S. corre o perigo de ser mais tarde vítima de cegueira, loucura, cardiopatias, esterilidade, ou outras consequências não menos graves.

O seu cartão de marinheiro identificá-lo-á em qualquer das clínicas ou hospitais mencionados na lista. Essas clínicas prestar-lhe-ão assistencia competente a pedido do Servico de Saúde Publica dos Estados Unidos.

Si Ud. sabe o cree que tiene sifilis (lúes) o blenorragia (gonorrea), preséntese en la clínica inscrita en este librito que le sea más conveniente, la próxima vez que baje Ud. a tierra. Si no se hace tratar ahora corre Ud. el peligro de ser más tarde víctima de ceguera, locura, enfermedad del corazón, esterilidad, u otras conscecuencias no menos graves.

Su ficha de marinero lo identificará en cualquiera de las clínicas u hospitales anotados en la lista. A solicitud del Servicio de Sanidad Pública de Estados Unidos esas clínicas le prestarán asistencia competente alguno para Ud.

Om Ni vet att Ni har syfilis eller gonorré (dröppel), eller om Ni misstänkar att Ni blivit smittad, anmäl Eder då genast, nästa gång Ni har landpermission, vid den närmaste av de kliniker som uppförts i förteckningen i denna bok. Om Ni inte låter behandla Eder genast, kan det leda till att Ni senare drabbas av blindhet eller sinnessjukdom, hjärtfel eller sterilitet (ofruktbarhet), eller av andra allvarliga och smärtsamma eftersjukdomar.

Ert sjömanskort är tillräcklig legitimation vid alla de kliniker och sjukhus som finnas i förteckningen. All behandling är ordnat för Eder av De förenta Staternas Public Health Service.

Dersom De vet at De har syfilis eller gonorré (dryppert), eller dersom De har mistanke om at De er blitt smittet, meld Dem da til behandling næste gang De har landlov ved den nærmeste av de klinikker som er oppført paa lista i denne boka. Dersom De forsømmer aa la Dem behandle naa

straks, kan det føre til at De senere i livet blir blind eller sinnssyk, faar hjertefeil, blir steril (ute av stand til aa avle barn), eller faar andre alvorlige og smertefulle ettersykdommer.

Deres sjømannskort vil være tilstrekkelig legitimasjon ved alle de klinikker eller hospitaler som er oppført paa lista. Behandlingen er ordna for Dem av De forenede Staters offentlige sundhetsvesen.

Dersom De ved at De har Syfilis eller Gonorre (Dryppert). eller dersom De har Mistanke om at De muligvis har været udsat for Smitte, meld Dem da til Behandling, næste Gang De har Landlov, ved den nærmeste af de Kliniker der er opført i Fortegnelsen i denne Bog. Dersom de forsømmer at lade Dem behandle nu straks, kan det føre til at De senere hen bliver blind eller sindssyg, faar Hjærtefeil, bliver steril (ude af Stand til at avle Børn), eller faar andre alvorlige og smertefulde Eftersygdomme.
Deres Sømandskort vil være tilstrækkelig Legitimation ved alle Kliniker eller Hospitaler i Fortegnelsen. Behandlinger er arrangeret for Dem af De forenede Staters offentlige Sundhedsvæsen.

Если вам известно или вы предполагаете, что у вас сифилис или гоноррея, зайдите в ближайшую лечебницу, указанную в этой книге, когда вы следующий раз сойдете на берег. Если вы не сделаете этого теперь, то это упущение может вызвать слепоту, нервное расстройство, сердечные заболевания, стерильность или сможет иметь другие серьезные и плачевные последствия.

Предъявите в указанных лечебницах или госпиталях вашу матросскую книжку - это все что требуется. Эти лечебные заведения обслуживают вас по поручению органов здравоохранения Соединенных Штатов Америки.

CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
	ALBANY, NEW YORK						
ALBANY NEW YORK	ALBANY HOSPITAL NEW SCOTLAND AVE	ALL	✓	✓	✓	✓	
ALBANY NEW YORK	MEMORIAL HOSPITAL 714 BROADWAY	ALL	✓	✓	✓	✓	
ALBANY NEW YORK	ST PETERS HOSPITAL NEW SCOTLAND AVE	ALL	✓	✓	✓		
	ALHAMBRA, CALIFORNIA						
ALHAMBRA CALIFORNIA	HEALTH CENTER 612 WEST SHORB ST	ALL	✓	✓	✓		
	APALACHICOLA, FLORIDA						
APALACHICOLA FLORIDA	COUNTY HEALTH DEPT	ALL	✓		✓		
	AZUSA, CALIFORNIA						
AZUSA CALIFORNIA	HEALTH CENTER 160 AZUSA ST	ALL	✓	✓	✓		
	BALBOA HEIGHTS, CANAL ZONE						
BALBOA HEIGHTS CANAL ZONE	U S P H S OUT PT OFC	ALL	✓	✓			✓

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R - EMPLOYEE OR INSTITUTIONAL GROUP AS INDICATED IN TITLE OF CLINIC

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CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
	BALTIMORE, MARYLAND						
BALTIMORE MARYLAND	CITY CLINIC NO 1 MUNICIPAL BLDG	A	✓	✓	✓		
BALTIMORE MARYLAND	CITY CLINIC NO 2 1313 DRUID HILL AVE	NM	✓	✓	✓		
BALTIMORE MARYLAND	CITY CLINIC NO 3 28 SOUTH BROADWAY	WM	✓	✓	✓		
BALTIMORE MARYLAND	CITY CLINIC NO 4 419 N BOND ST	NM	✓	✓	✓		
BALTIMORE MARYLAND	CITY CLINIC NO 6 1313 DRUID HILL AVE	N	✓		✓		
BALTIMORE MARYLAND	EYE EAR THROAT HOSP EUTAW AND LANVALE	ALL	✓			✓	
BALTIMORE MARYLAND	CITY CLINIC NO 7 1313 DRUID HILL AVE	N M	✓		✓		
BALTIMORE MARYLAND	GU DISP JNO HOPKINS BROADWAY AT MONUMENT	M		✓		✓	
BALTIMORE MARYLAND	JOHNS HOPKINS HOSP BROADWAY AT MONUMENT	ALL	✓			✓	
BALTIMORE MARYLAND	MERCY HOSPITAL CALVERT AND SARATOGA	A	✓	✓			✓
BALTIMORE MARYLAND	SINAI HOSPITAL MONUMENT AND RUTLAND	W	✓	✓		✓	✓
BALTIMORE MARYLAND	S BALTIMORE GEN HOSP LIGHT STREET	ALL	✓	✓			✓
BALTIMORE MARYLAND	UNIVERSITY HOSPITAL LOMBARD AND GREEN						
BALTIMORE MARYLAND	U S MARINE HOSPITAL WYMAN PK DR AND 31ST	ALL	✓	✓			✓
BALTIMORE MARYLAND	U S P H S OUT PT OFC GAY AND WATER STS	ALL	✓	✓			✓
BALTIMORE MARYLAND	W BALTIMORE GEN HOSP RAYNOR AND DUKELAND	W	✓	✓			✓
	BEAUMONT, TEXAS						
BEAUMONT TEXAS	V D CLINIC 855 TRINITY ST	ALL	✓	✓	✓		

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W - WHITES ONLY A - ADULTS ONLY M - MALES ONLY R - EMPLOYEE OR INSTITUTIONAL GROUP

N - NEGROES ONLY C - CHILDREN ONLY F - FEMALES ONLY AS INDICATED IN TITLE OF CLINIC

CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
	BOSTON, MASSACHUSETTS						
BOSTON MASSACHUSETTS	BOSTON DISPENSARY 25 BENNET ST	ALL	✓	✓	✓	✓	✓
BOSTON MASSACHUSETTS	MASS GENERAL HOSP FRUIT ST	ALL	✓	✓	✓	✓	✓
BOSTON MASSACHUSETTS	U S MARINE HOSPITAL 77 WARREN STREET	ALL	✓	✓			✓
BOSTON MASSACHUSETTS	U S P H S OUT PT OFC CUSTOM HSE INDIA ST	ALL	✓	✓			✓
	BRONX (SEE NEW YORK CITY)						
	BROOKLYN (SEE NEW YORK CITY)						
	BROWNSVILLE, TEXAS						
BROWNSVILLE TEXAS	COUNTY CLINIC CITY HALL	ALL	✓	✓	✓		
	BRUNSWICK, GEORGIA						
BRUNSWICK GEORGIA	CITY CLINIC	ALL	✓	✓	✓		
	BURBANK, CALIFORNIA						
BURBANK CALIFORNIA	HEALTH CENTER 528 NORTH OLIVE ST	ALL	✓	✓	✓		

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CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
	CHARLESTON, SOUTH CAROLINA						
CHARLESTON SOUTH CAROLINA	HEALTH CENTER CLINIC HEALTH DEPT	ALL	✓	✓	✓		
CHARLESTON SOUTH CAROLINA	ROPERS HOSPITAL LUCAS AND CALHOUN	ALL	✓			✓	✓
CHARLESTON SOUTH CAROLINA	U S P H S OUT PT OFC E BAY AND MARKET	ALL	✓	✓			✓
	COMPTON, CALIFORNIA						
COMPTON CALIFORNIA	HEALTH CENTER 1301 WILLOWBROOK AVE	ALL	✓	✓	✓		
	CORPUS CHRISTIE, TEXAS						
CORPUS CHRISTI TEXAS	CITY CLINIC CLINIC BLDG	ALL	✓	✓	✓		
	EAST LOS ANGELES, CALIFORNIA						
EAST LOS ANGELES CALIFORNIA	HEALTH CENTER 670 SOUTH FERRIS ST	ALL	✓	✓	✓		
	ELLIS ISLAND (SEE NEW YORK CITY)						
	EL MONTE, CALIFORNIA						
EL MONTE CALIFORNIA	HEALTH CENTER 333 CALIFORNIA ST	ALL	✓	✓	✓		

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CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
	FAR ROCKAWAY (SEE NEW YORK CITY)						
	FLUSHING (SEE NEW YORK CITY)						
	GALVESTON, TEXAS						
GALVESTON TEXAS	JOHN SEALY HOSPITAL UNIVERSITY OF TEXAS	ALL	✓	✓	✓		
GALVESTON TEXAS	U S MARINE HOSPITAL 45TH AND AVENUE N	ALL	✓	✓			✓
GALVESTON TEXAS	U S P H S OUT PT OFC 17TH AVENUE B	ALL	✓	✓			✓
	GLENDALE, CALIFORNIA						
GLENDALE CALIFORNIA	HEALTH CENTER 200 W LEXINGTON DR	ALL	✓	✓	✓		
	HOUSTON, TEXAS						
HOUSTON TEXAS	CITY CLINIC NO 1 OLD JEFF DAVIS HOSP	ALL	✓	✓	✓		
HOUSTON TEXAS	CITY V D CLINIC NO 2 HEALTH CENTER NO 2	ALL	✓	✓	✓		
HOUSTON TEXAS	CITY V D CLINIC NO 3 HEALTH CENTER NO 3	ALL	✓	✓	✓		

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CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
	HUNTINGTON PARK, CALIFORNIA						
HUNTINGTON PARK CALIFORNIA	SAN ANTONIO H CENTER 7300 SANTA FE AVE	ALL	✓	✓	✓		
	INGLEWOOD, CALIFORNIA						
INGLEWOOD CALIFORNIA	HEALTH CENTER 101 S GREVILLEA ST	ALL	✓	✓	✓		
	JACKSONVILLE, FLORIDA						
JACKSONVILLE FLORIDA	DUVAL CO HOSPITAL 710 W 10TH ST	ALL	✓	✓	✓		
	JAMAICA (SEE NEW YORK CITY)						
	KEY WEST, FLORIDA						
KEY WEST FLORIDA	COUNTY HEALTH DEPT 1300 UNITED ST	ALL	✓	✓	✓		
	LANCASTER, CALIFORNIA						
LANCASTER CALIFORNIA	HEALTH CENTER 311 WEST 10TH ST	ALL	✓	✓	✓		

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CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
	LONG BEACH, CALIFORNIA						
LONG BEACH CALIFORNIA	CITY HEALTH DEPT 404 CITY HALL	ALL	✓	✓	✓		
	LOS ANGELES, CALIFORNIA						
LOS ANGELES CALIFORNIA	MENS CENTRAL CLINIC 116 TEMPLE ST RM 200	M	✓	✓	✓		
LOS ANGELES CALIFORNIA	SOUTHEAST POLYCLINIC CENTRAL AVE AT 55 ST	N	✓	✓	✓		
LOS ANGELES CALIFORNIA	WEST L A CLINIC 1620 PURDUE AVE	ALL	✓	✓	✓		
LOS ANGELES CALIFORNIA	US P H S OUT PT OFC SPRING AND TEMPLE	ALL	✓	✓			✓
	MANHATTAN, (SEE NEW YORK CITY)						
	MIAMI, FLORIDA						
MIAMI FLORIDA	CITY CLINIC 910 COURTHOUSE	ALL	✓	✓	✓	✓	
MIAMI FLORIDA	DADE CO HOSPITAL ROUTE 2	ALL	✓	✓	✓		
MIAMI FLORIDA	U S P H S OUT PT OFC 1ST AVE AT 3RD ST NE	ALL	✓	✓			✓
	MOBILE, ALABAMA						
MOBILE ALABAMA	COUNTY CLINIC CITY HOSPITAL	ALL	✓	✓	✓		
MOBILE ALABAMA	U S MARINE HOSPITAL ST ANTHONY AND BAYOU	ALL	✓	✓			✓

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CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
	MONROVIA, CALIFORNIA						
MONROVIA CALIFORNIA	HEALTH CENTER 211 W COLORADO BLVD	ALL	✓	✓	✓		
	NEW ORLEANS, LOUISANA						
NEW ORLEANS LOUISIANA	CHARITY HOSPITAL 1532 TULANE AVE	ALL	✓	✓	✓		
NEW ORLEANS LOUISIANA	FLINT GOODRIDGE CLIN 2425 LOUISIANA AVE	N	✓	✓	✓		
NEW ORLEANS LOUISIANA	HUTCHINSON MEM HOSP TULANE AVE	ALL	✓	✓	✓		
NEW ORLEANS LOUISIANA	ISOLATION HOSP 513 N RAMPART ST	ALL	✓	✓	✓		
NEW ORLEANS LOUISIANA	TOURO INFIRMARY 3516 PRYTANIA ST	ALL	✓	✓	✓	✓	
NEW ORLEANS LOUISIANA	U S MARINE HOSPITAL 210 STATE ST	ALL	✓	✓			✓
NEW ORLEANS LOUISIANA	U S P H S OUT PT OFC 423 CANAL STREET	ALL	✓	✓			✓
NEW ORLEANS LOUISIANA	V D CONTROL DIVISION CITY HALL ANNEX	ALL	✓	✓	✓		
	NEWPORT NEWS, VIRGINIA						
NEWPORT NEWS VIRGINIA	V D CLINIC 2516 WASHINGTON ST	ALL	✓	✓	✓		
NEWPORT NEWS VIRGINIA	WHITTAKER HOSP OPD 1014 29TH ST	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
	NEW YORK CITY						
BOROUGH OF THE BRONX							
NEW YORK NEW YORK	FORDHAM HOSPITAL SOUTHERN AND CROTONA	ALL	✓	✓	✓		
NEW YORK NEW YORK	LINCOLN HOSPITAL 141ST AND CONCORD	ALL	✓	✓	✓		
NEW YORK NEW YORK	MORRISANIA HOSPITAL 168TH AND GERARD	ALL	✓	✓	✓		
NEW YORK NEW YORK	MOTT HAVEN H CENTER 349 E 140TH ST	ALL	✓	✓	✓		
NEW YORK NEW YORK	TREMONT CLINIC 1826 ARTHUR AVE	ALL	✓	✓	✓		
BOROUGH OF BROOKLYN							
BROOKLYN NEW YORK	BUSHWICK H CENTER 186 GROVE ST	ALL	✓	✓	✓		
BROOKLYN NEW YORK	FT GREENE SOC HYG CL 295 FLATBUSH AVE EXT	ALL	✓	✓	✓		
BROOKLYN NEW YORK	GREENPOINT HOSPITAL KINGSLAND AVE	ALL	✓	✓	✓		
BROOKLYN NEW YORK	KINGS CO HOSPITAL 451 CLARKSON AVE	ALL	✓	✓	✓		
BROOKLYN NEW YORK	RED HOOK GOWANUS CL 250 BALTIC ST	ALL	✓	✓	✓		
BROOKLYN NEW YORK	WMSBURG GREENPT CL 151 MAUJER ST	ALL	✓	✓	✓		
ELLIS ISLAND							
ELLIS ISLAND NEW YORK	U S MARINE HOSPITAL	ALL	✓	✓			✓
BOROUGH OF QUEENS (INCLUDES FLUSHING, FAR ROCKAWAY, & JAMAICA)							
FAR ROCKAWAY L I NEW YORK	CITY CLINIC 1517 CENTRAL AVE	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
FLUSHING L I NEW YORK	FLUSHING CORONA CLI 3433 JUNCTION BLVD	ALL	✓	✓	✓		
JAMAICA L I NEW YORK	JAMAICA WEST CLINIC 9218 149TH ST	ALL	✓	✓	✓		
JAMAICA L I NEW YORK	QUEENS GENERAL HOSP 161ST ST ANU 82ND DR	ALL	✓	✓	✓		
BOROUGH OF MANHATTAN							
NEW YORK NEW YORK	BELLEVUE HOSP CLINIC 1ST AVE AND 26TH ST	ALL	✓	✓	✓		
NEW YORK NEW YORK	CENTRAL CLINIC 130 LEONARD ST	ALL	✓	✓	✓		
NEW YORK NEW YORK	CEN HARLEM CLINIC 2238 FIFTH AVE	ALL	✓	✓	✓		
NEW YORK NEW YORK	CITY HOSP DISP 535 EAST 80TH ST	ALL	✓	✓	✓		
NEW YORK NEW YORK	EAST HARLEM CLINIC 158 E 115TH ST	ALL	✓	✓	✓		
NEW YORK NEW YORK	GOUVERNEUR HOSP GOUVERNEUR SLIP	ALL	✓	✓	✓		
NEW YORK NEW YORK	HARLEM HOSPITAL 136TH ST AT LENOX AV	ALL	✓	✓	✓		
NEW YORK NEW YORK	LOWER W SIDE CLINIC 303 NINTH AVE	ALL	✓	✓	✓		
NEW YORK NEW YORK	MEINHARD CLINIC 130 EAST 101ST ST	ALL	✓	✓	✓		
NEW YORK NEW YORK	METROPOLITAN DISP 535 E 80TH ST	ALL	✓	✓	✓		
NEW YORK NEW YORK	U S MARINE HOSPITAL 67 HUUSON STREET	ALL	✓	✓			✓
NEW YORK NEW YORK	U S P H S OUT PT OFC BARGE OFF SO FERRY	ALL	✓	✓			✓
NEW YORK NEW YORK	WASHINGTON CLINIC 128 PRINCE ST	ALL	✓	✓	✓		
NEW YORK NEW YORK	WASH HTS SOC HYG CL 600 WEST 168TH ST	ALL		✓	✓		

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			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
BOROUGH OF RICHMOND (INCLUDES STATEN ISLAND)							
STATEN ISLAND NEW YORK	OLD COURT HOUSE CL 302 CENTER AVE	ALL	✓	✓	✓		
STATEN ISLAND NEW YORK	RICHMOND V D CLINIC 51 STUYVESANT PLACE	ALL	✓	✓	✓		
STATEN ISLAND NEW YORK	U S MARINE HOSPITAL STAPLETON	ALL	✓	✓			✓
	NORFOLK, VIRGINIA						
NORFOLK VIRGINIA	CO MED SOC CLINIC HEALTH DEPARTMENT	ALL	✓	✓	✓		
NORFOLK VIRGINIA	PUBLIC CLINIC 449 EAST BUTE ST	N	✓	✓	✓	✓	
NORFOLK VIRGINIA	U S MARINE HOSPITAL HAMPTON BLVD	ALL	✓	✓			✓
NORFORK VIRGINIA	U S P H S OUT PT OFC GRANBY AND MAINE	ALL	✓	✓			✓
	OAKLAND, CALIFORNIA						
OAKLAND CALIFORNIA	CITY CLINIC 282 EIGHTH ST	ALL	✓	✓	✓		
	PANAMA CITY, FLORIDA						
PANAMA CITY FLORIDA	COUNTY HEALTH DEPT 315 MCKENZIE AVE	ALL	✓	✓	✓		
	PENSACOLA, FLORIDA						
PENSACOLA FLORIDA	COUNTY HEALTH DEPT 803 N PALAFOX ST	ALL	✓	✓	✓		

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			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
	PHILADELPHIA, PENNSYLVANIA						
PHILADELPHIA PENNSYLVANIA	BARTON DISPENSARY 21ST AND NO COLLEGE	ALL	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	BROAD ST HOSPITAL 733 SOUTH BROAD ST	ALL	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	COMMUNITY HOSPITAL 10TH AND CARPENTER	ALL	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	DOUGLAS HOSPITAL 1530 LOMBARD ST	N	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	FRANKFORD HOSP O P D FRANKFORD AVE	ALL	✓	✓	✓	✓	
PHILADELPHIA PENNSYLVANIA	GERMANTOWN HOSPITAL PENN AND CHEW STS	ALL	✓	✓		✓	
PHILADELPHIA PENNSYLVANIA	HAHNEMANN HOSPITAL BROAD ST ABOVE RACE	ALL	✓		✓	✓	
PHILADELPHIA PENNSYLVANIA	JEFFERSON HOSPITAL 10TH AND SANSOM STS	ALL	✓	✓	✓	✓	
PHILADELPHIA PENNSYLVANIA	JEWISH HOSPITAL YORK AND TABOR RD	ALL	✓	✓		✓	
PHILADELPHIA PENNSYLVANIA	MERCY HOSPITAL 5000 WOODLAND AVE	ALL	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	METH EPISC HOSP BROAD AND WOLF STS	ALL	✓			✓	
PHILADELPHIA PENNSYLVANIA	PENNSYLVANIA HOSP 8TH AND SPRUCE STS	ALL	✓	✓	✓	✓	
PHILADELPHIA PENNSYLVANIA	PRESBYTERIAN HOSP 39TH ST AT POWELTON	ALL	✓	✓	✓	✓	
PHILADELPHIA PENNSYLVANIA	ST AGNES HOSPITAL BROAD AND MIFLIN STS	ALL	✓	✓		✓	
PHILADELPHIA PENNSYLVANIA	ST JOSEPHS HOSP 16TH ST AT GIRARD	ALL	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	ST LUKES HOSPITAL 8TH AND THOMPSON STS	ALL	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	ST MARYS HOSPITAL FRANKFORD AT PALMER	ALL	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	SKIN AND CANCER HOSP 802 PINE ST	ALL	✓		✓	✓	
PHILADELPHIA PENNSYLVANIA	STATE CLINIC 1137 SOUTH 20TH ST	ALL	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	STATE CLINIC 1129 CALLOWHILL ST	ALL	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	STETSON HOSPITAL 1745 NO 4TH ST	ALL	✓	✓	✓		
PHILADELPHIA PENNSYLVANIA	TEMPLE MED SCHOOL BROAD AND ONTARIO ST	ALL	✓			✓	
PHILADELPHIA PENNSYLVANIA	UNIV OF PENNA HOSP 34TH AND SPRUCE STS	ALL	✓			✓	

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			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
PHILADELPHIA PENNSYLVANIA	U S P H S OUT PT OFC 225 CHESTNUT ST	ALL	✓	✓			✓
PHILADELPHIA PENNSYLVANIA	V D CLINIC 20TH AND BERKS STS	ALL	✓	✓	✓		
	POMONA, CALIFORNIA						
POMONA CALIFORNIA	HEALTH CENTER 280 WEST FIFTH ST	ALL	✓	✓	✓		
	PORT ARTHUR, TEXAS						
PORT ARTHUR TEXAS	CITY CLINIC CITY HALL	ALL	✓	✓	✓		
	PORT ISABEL, TEXAS						
PORT ISABEL TEXAS	CITY CLINIC DR HOCKADAYS OFFICE	ALL	✓	✓	✓		
	PORTLAND, MAINE						
PORTLAND MAINE	STATE V D CLINIC 65 INDIA ST	ALL	✓	✓		✓	
PORTLAND MAINE	STATE V D CLINIC M EYE EAR INFIRMARY	ALL	✓	✓	✓		
PORTLAND MAINE	U S MARINE HOSPITAL 331 VERANDA AVE	ALL	✓	✓			✓

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			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
	PORTLAND, OREGON						
PORTLAND OREGON	OREGON UNIV MED SCH 3181 SW MARQUAM HILL	ALL	✓	✓	✓	✓	✓
PORTLAND OREGON	PUBLIC HEALTH CLINIC 231 S W THIRD AVE	ALL	✓	✓	✓		
PORTLAND OREGON	U S P H S OUT PT OFC 520S W MORRISONST	ALL	✓	✓			✓
	PORTSMOUTH, VIRGINIA						
PORTSMOUTH VIRGINIA	CITY HEALTH DEPT NEW MARKET BUILDING	ALL	✓	✓	✓		
PORTSMOUTH VIRGINIA	PUBLIC V D CLINIC 401 SOUTH GREEN ST	ALL	✓		✓	✓	
	PRITCHARD, ALABAMA						
PRITCHARD ALABAMA	COUNTY CLINIC CITY HALL ANNEX	ALL	✓	✓	✓		
	PROVIDENCE, RHODE ISLAND						
PROVIDENCE RHODE ISLAND	C V CHAPIN HOSP 153 EATON ST	ALL	✓	✓	✓	✓	
	RICHMOND (SEE NEW YORK CITY)						

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			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
	SAN DIEGO, CALIFORNIA						
SAN DIEGO CALIFORNIA	MUNICIPAL CLINIC CIVIC CENTER	ALL	✓	✓	✓		
SAN DIEGO CALIFORNIA	U S P H S OUT PT OFC 9TH AVE AT E ST	ALL	✓	✓			✓
	SAN FERNANDO, CALIFORNIA						
SAN FERNANDO CALIFORNIA	HEALTH CENTER 604 MACLAY AVE	ALL	✓	✓	✓		
	SAN FRANCISCO, CALIFORNIA						
SAN FRANCISCO CALIFORNIA	CITY HEALTH DEPT 33 HUNT ST	ALL	✓	✓	✓		
SAN FRANCISCO CALIFORNIA	U S MARINE HOSPITAL 14TH AND PARK BLVD	ALL	✓	✓			✓
SAN FRANCISCO CALIFORNIA	U S P H S OUT PT OFC 5TH AND MISSION STS	ALL	✓	✓			✓
SAN FRANCISCO CALIFORNIA	U S P H S OUT PT OFC OLD MINT BLDG	ALL	✓	✓			✓
	SAN PEDRO, CALIFORNIA						
SAN PEDRO CALIFORNIA	CITY CLINIC 599 WEST SEVENTH ST	ALL	✓	✓	✓		
SAN PEDRO CALIFORNIA	U S P H S OUT PT OFC BEACON AT NINTH	ALL	✓	✓			✓
	SANTA MONICA, CALIFORNIA						
SANTA MONICA CALIFORNIA	HEALTH CENTER 1525 EUCLID ST	ALL	✓	✓	✓		

* WHEN SERVICE IS LIMITED, RESTRICTIONS ARE INDICATED AS FOLLOWS:

W - WHITES ONLY A - ADULTS ONLY M - MALES ONLY R - EMPLOYEE OR INSTITUTIONAL GROUP

N - NEGROES ONLY C - CHILDREN ONLY F - FEMALES ONLY AS INDICATED IN TITLE OF CLINIC

CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA	FREE	PART-PAY.	PAY
	SAVANNAH, GEORGIA						
SAVANNAH GEORGIA	CITY CLINIC	ALL	✓	✓	✓		
SAVANNAH GEORGIA	U S MARINE HOSPITAL YORK AND ABERCORN	ALL	✓	✓			✓
	SEATTLE, WASHINGTON						
SEATTLE WASHINGTON	HEALTH DEPT CLINIC 416 YESLER WAY	ALL	✓	✓	✓	✓	
SEATTLE WASHINGTON	U S MARINE HOSPITAL JUDKINS AT 14TH AVE	ALL	✓	✓			✓
SEATTLE WASHINGTON	U S P H S OUT PT OFC 909 FIRST AVE	ALL	✓	✓			✓
	STATEN ISLAND (SEE NEW YORK CITY)						
	TACOMA, WASHINGTON						
TACOMA WASHINGTON	TACOMA P H CLINIC 322 PROVIDENT BLDG	ALL	✓	✓	✓	✓	
	TAMPA, FLORIDA						
TAMPA FLORIDA	CO HEALTH DEPT 1301 FLORIDA AVENUE	ALL	✓	✓	✓		
TAMPA FLORIDA	V D CLINIC 1420 TAMPA ST	ALL	✓	✓	✓		

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CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPHILIS	GONORRHEA	FREE	PART-PAY.	PAY
	TORRANCE, CALIFORNIA						
TORRANCE CALIFORNIA	HEALTH CENTER 2300 CARSON ST	ALL	✓	✓	✓		
	VAN NUYS, CALIFORNIA						
VAN NUYS CALIFORNIA	V D CLINIC 14410 SYLVAN ST	ALL	✓	✓	✓		
	VENICE, CALIFORNIA						
VENICE CALIFORNIA	V D CLINIC 685 VENICE BLVD	ALL	✓	✓	✓		
	VIRGINIA BEACH, VIRGINIA						
VIRGINIA BEACH VIRGINIA	CITY CLINIC HEALTH CENTER	ALL	✓	✓	✓		
	WATTS, CALIFORNIA						
WATTS CALIFORNIA	V D CLINIC FOR MEN CITY HALL	M	✓	✓	✓		
	WEST HOLLYWOOD, CALIFORNIA						
WEST HOLLYWOOD CALIFORNIA	HEALTH CENTER 730 N SAN VINCENTE	ALL	✓	✓	✓		

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C - CHILDREN ONLY
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F - FEMALES ONLY
R - EMPLOYEE OR INSTITUTIONAL GROUP AS INDICATED IN TITLE OF CLINIC

CITY AND STATE	CLINIC NAME AND ADDRESS	SERVICE TO *	CLINIC TREATS		FEE SYSTEM		
			SYPH-ILIS	GONOR-RHEA.	FREE	PART-PAY.	PAY
	WHITTIER, CALIFORNIA						
WHITTIER CALIFORNIA	HEALTH CENTER 402 S GREENLEAF ST	ALL	✓	✓	✓		
	WILMINGTON, CALIFORNIA						
WILMINGTON CALIFORNIA	COUNTY V D CLINIC 212 F STREET	ALL	✓	✓	✓		

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MANAGEMENT OF SYPHILIS

IN GENERAL PRACTICE

By JOSEPH EARLE MOORE, M. D., *Johns Hopkins University*

In collaboration with: HAROLD N. COLE, M. D.
Western Reserve University

PAUL A. O'LEARY, M. D.
Mayo Clinic

THOMAS PARRAN
Surgeon General
U. S. Public Health Service

JOHN H. STOKES, M. D.
University of Pennsylvania

R. A. VONDERLEHR
Assistant Surgeon General
U. S. Public Health Service

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THE MANAGEMENT OF

SYPHILIS

IN GENERAL PRACTICE[1]

• **If syphilis is to be controlled,** every physician in the United States must cooperate . . .
(a) In diagnosis of the disease among his own patients . . .
(b) In perfecting himself in methods of treatment for the uncomplicated case, or, if he does not care to do this, in referring his syphilitic patients to other physicians skilled in treatment methods.

SYPHILIS in the United States is the most prevalent of the major communicable diseases. Its relative annual incidence here, and in Denmark, Sweden, and Great Britain may be seen in figure 1. The fact that there is from 50 to 100 times as much syphilis here as in these countries cannot be explained on the grounds of local increased virulence of the organism,

[1] This article revises and expands the article The Management of Syphilis in General Practice, by J. E. Moore, H. N. Cole, J. G. Schamberg, H. C. Solomon, U. J. Wile, and J. H. Stokes, which was published in Venereal Disease Information, 1929, v. 10, p. 53 and also as Reprint No. 13 from Venereal Disease Information. Portions of the present article are direct repetitions, though there is much new material based on recent studies.

NOTE.—The authors of this article are members of the Cooperative Clinical Group.

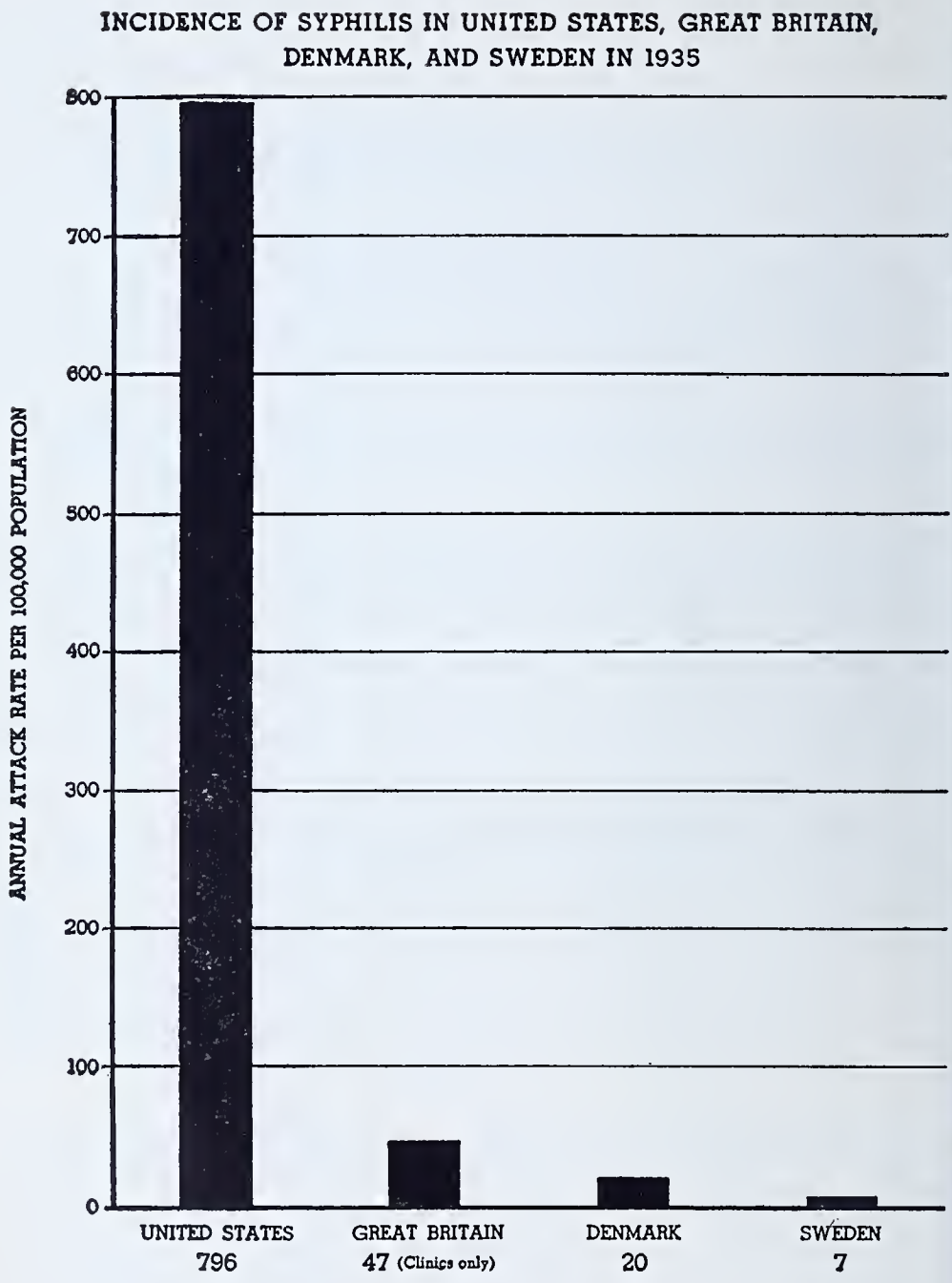

FIGURE 1

decreased resistance in the host, or greater sexual promiscuity among our people. What then does account for it? The answer is inescapable—failure of the medical profession and of health officers to cope as adequately with syphilis as with other communicable diseases. The major failure is made up of several parts: Inability, even in the minds of physi-

cians, to dissociate morals and medicine; inability to diagnose syphilis; inability to treat it properly once it has been diagnosed.

In Scandinavia and Great Britain, the management of syphilis has been, for the past quarter century, largely a function of the State. Treatment is free to all, and is centralized in the hands of a few experts. These facts are in part responsible for their success.

In the United States, it is not only undesirable but also, because of political diversification, probably impossible for the State to assume the burden to the extent practiced abroad. Further, it is unnecessary for the State to do so, *if the medical profession will do its part.*

The public health attack on syphilis differs from that on any other communicable disease. It cannot be made by the health officer alone, as in the eradication of typhoid fever, smallpox, and diphtheria. The contact which causes syphilis cannot be prevented; there is no intermediate host to exterminate; immunization will not work; quarantine is impossible. It cannot be made by any group of experts working alone. There are too many patients (about 10,000,000 in the United States) and too few experts—a few thousand at a generous estimate. Moreover, as will be presently emphasized, syphilis may attack any organ in the body, and in most cases the patient must be recognized as syphilitic by his family physician or consulting specialist before he reaches the hands of the expert syphilologist.

The attack cannot be made even by the medical profession alone. Law enforcement officers engaged in the suppression of prostitution, educators concerned with the sex education of children, agencies providing substitutive recreational activities, the clergy, all have their part. So far as physicians are concerned, however, two points seem clear if the fight is to be won:

1. The doctor should confine himself to the medical aspects of the situation, leaving other phases of it to those better qualified.

2. *Every doctor must be prepared to play his part.* What that part is will be made clear in the discussion of the three major elements of the control program, prophylaxis, diagnosis, and treatment.

THE PROPHYLAXIS OF SYPHILIS

THE *social* prophylaxis of venereal disease is, so far as law enforcement, educational, substitutive, and religious activities are concerned, more properly the task of other agencies than the medical profession. Nevertheless, these agencies will not be able to act intelligently unless they are provided by physicians with accurate knowledge of venereal diseases, and such knowledge should likewise be made freely available to the general public. The campaign against syphilis is handicapped, as that against

tuberculosis was not, by the fact that syphilis is usually acquired by sexual contact, illicit as well as within marriage. Not only the public but a part of the medical profession as well must get over the idea that syphilis is punishment for sin, that it must be disguised by the phrase "social disease," that it is shameful, if headway is to be made in stamping it out.

The physician should bear his fair proportion in the community burden of proper sex instruction in the schools, of providing adequate facilities for recreation for adolescents, of suppressing legalized prostitution, of educating the press to an intelligent attitude toward venereal disease.

It must be remembered that if promiscuous sexual contacts can be decreased, venereal diseases will decrease proportionately. The physician can do much to dispel the old superstition that continence is incompatible with good health, to emphasize that every illicit sexual exposure is a potential source of infection with gonorrhea, chancroid, or syphilis, and that the most effective prophylaxis is abstinence from promiscuous sexual contact. However, since this is not a fully attainable ideal, other measures to prevent the development of disease after exposure should be utilized.

Medical measures of prophylaxis may be classified as chemical, chemotherapeutic, and mechanical.

Chemical Prophylaxis

This is really early treatment applied before the organisms have had time to penetrate the tissues. It can prevent infection with all venereal diseases if properly applied and if used early enough. It is most effective if applied within an hour after exposure (the first exposure of the series, not the last), and rapidly decreases in value as the interval between exposures and treatment lengthens. It is still of some value, especially against syphilis, as late as 8 hours after exposure.

Under conditions of military control, especially in our own Army and Navy, chemical prophylaxis has been brilliantly successful in reducing the incidence of venereal disease to a remarkedly low level. Unfortunately, in civilian life it is practically unworkable since men will not take it except under compulsion. Nevertheless, every physician should know the steps in the technic.

Technic of prophylaxis for the male.—If possible do not allow the patient to administer the treatment to himself. The patient is made to urinate. He is provided with a basin of warm water and a gauze wipe, with which he washes the genitals thoroughly while liquid green soap is dropped on the penis. The washing to be done thoroughly should consume about 10 minutes and should include the penis, scrotum, pubis, and the adjacent areas of the thighs. Use especial care to wash thoroughly the folds of the frenum and foreskin. After washing, the parts should be dried thoroughly. The washing with soap and water is important; soap is the only part of the treatment effective against

chancroid, and is also of value as a destroyer of the organism of syphilis. Before proceeding further the presence of urethral discharge or genital sores is noted.

The next step is the injection of 1 dram (4 cc) of a freshly made 2 percent protargol solution (or a 10 percent solution of argyrol) into the urethra by the physician. The patient then holds the meatus firmly between the thumb and forefinger for 5 minutes, from time to time allowing a drop to escape from the meatus so that all parts of the urethra are in contact with the solution. At the end of 5 minutes the protargol is allowed to escape, without pressure or stripping, so that a few drops remain. One-half to 1 dram (2 to 4 grams) of 33 percent calomel ointment is next rubbed thoroughly by the patient, under the observation of the physician, into all parts of the penis for 5 minutes, special attention being paid to the retracted prepuce, the frenum, and the glans. The scrotum also should be rubbed with ointment. The genitalia are then wrapped in toilet paper or waxed paper to protect the clothes, and the patient is instructed not to urinate for four or five hours.

The formulae for calomel ointment used in the United States Army and Navy, which have proved their efficacy, are as follows:

United States Army	*Parts*
Hydrargyri chloridum mite	30
Adeps benzoinatus	65
Cera alba U. S. P	5

United States Navy	*Parts*
Calomel	33
Camphor	2
Phenol	3
Anhyd. lanolin	39
Benz. lard	20
Beeswax	3

Remember that soap and water is protection against chancroid and partially against syphilis, protargol against gonorrhea, and calomel ointment probably only against syphilis.

Before and since the war an extensive search has been made for one drug or a combination which might prove effective against all three diseases, but so far without satisfactory results.

If prophylactic treatment under the direction of a physician is not available, it is worth while for the patient to be advised to use one of the individual prophylactic packets put out by various commercial houses, directions for the use of which usually accompany the packet. Though this is not as satisfactory as the scheme outlined above, the experience of the United States Navy and the Australian and New Zealand troops during the war indicate that it is of some value; and the prevention of only a single case of syphilis is a worth-while accomplishment.

Technic of prophylaxis for the female.—In cases of rape, and in some others, there may be occasion for applying early treatment to females. If such occasion should arise, the following procedure is suggested: Have the patient urinate. Place the patient in the lithotomy position. Wash the genitals and adjacent parts with soap and water. Give a douche of 2 quarts of sterile water, temperature 100° F., followed by 2 quarts of 1:2000 mercuric chloride solution, and wash external parts with the latter. Dry the vagina and vulva by sponging. Swab the entire vagina, through a speculum, with a 2 percent protargol solution, or 10 percent argyrol solution, freshly made; reach every fold and especially the posterior vault and external os. Swab the entire vulva in the same way,

reaching every recess. Inject enough of the same solution into the urethra to distend it moderately and let the patient hold her finger (in a rubber glove) against the meatus to retain the solution for from 3 to 5 minutes.

Douche the vagina and vulva with a small amount of sterile water, and sponge dry with gauze. Apply calomel ointment to the cervix, vagina, vulva and adjacent parts, rubbing thoroughly into the recesses and folds of the mucous membranes and skin, and taking at least 10 minutes for the operation. Do not use more than 4 grams (1 dram) of calomel ointment in the vagina. Cover the external parts securely with oiled silk or waxed paper, and instruct the patient to allow ointment to remain for several hours before washing the parts.

The civilian substitute for the Army technic is the prophylactic tube, of which several varieties are on general sale. All of them depend on the incorporation in a single ointment base, dispensed in a collapsible tube, of a combination of chemicals supposedly effective against both gonorrhea and syphilis. Although the user of this tube may not dispense with the preliminary thorough washing with soap and water (which is probably as effective against syphilis as calomel ointment) and although phenol and the silver salts in an ointment base are not as efficient against gonorrhea as in aqueous solution, such tubes may do some good in prevention. Their sale should be encouraged, and research efforts to improve them continued.

Chemical prophylaxis has, however, a highly important place in the prevention of accidental infection with syphilis among doctors, nurses, and dentists. In the ordinary handling of infectious lesions, even if there are abrasions on the fingers, immediate thorough washing with soap and water is adequate protection. In the case of scratch or puncture wounds with infected instruments, the wound should be laid open with a sterile scalpel to the approximate depth of the puncture, and should be packed with 33 percent calomel ointment, which is allowed to stay in place for 24 hours under a sterile dressing.

Chemotherapeutic Prophylaxis

Three methods are advocated: (1) The oral use of stovarsol (synonyms, acetarsone, spirocide), a pentavalent arsenical, both before and after exposure; (2) frequently repeated intramuscular injections of bismuth during the active period when exposures may be expected to occur; (3) the intravenous injection of an arsphenamine after exposure.

Stovarsol may be dismissed from present consideration because the case for it is not yet proved, and because the drug is too toxic.

Bismuth prophylaxis, applicable to groups of prostitutes, is obviously useless in ordinary practice, since it is tantamount to the continuous antisyphilitic treatment of noninfected persons.

The proposals for arsphenamine prophylaxis are so far limited to those individuals exposed to a known infectious syphilitic. If this somewhat

unusual situation arises, and if one or several injections of arsphenamine can be given within 48 (preferably 24 hours) after exposure, it is claimed that the development of syphilis may be prevented. While this is true in the experimental animal, the value of the procedure in man is still debatable. It is open to the objection that if it is carried out, the infection may be only suppressed instead of eradicated. In any case, both physician and patient are in the difficult position of not knowing whether or not the patient would have acquired the disease if not so treated. On the other hand, it is probable that under these circumstances, if infection actually has occurred, it may be "cured" with more certainty and with less treatment than if one waits for lesions or a positive blood serologic test to appear. On the whole, the controversy between the advocates and opponents of this plan may be compromised by putting the question squarely up to the patient as follows: "Since you have been exposed to a known infectious syphilitic, it is probable though not certain that you have acquired the disease. If you have acquired it, it can be 'cured' more easily and with less treatment if you start immediately than if you wait for lesions to appear. But, if you take treatment now, you must regard yourself as a syphilitic, and though you have been more fortunate than most in that your treatment was begun very early, you must be followed for a lifetime of observation, exactly as if you had developed lesions."

If the patient chooses early prophylactic treatment, (1) it should not be given later than 48 hours after the suspected exposure; (2) it should consist, not of one or two arsphenamine injections, but of at least one complete arsphenamine course (8 arsphenamine or 10 neoarsphenamine or silver-arsphenamine), followed by a course of bismuth or mercury; (3) the patient should be followed with monthly blood serologic tests for the first year, every 2 or 3 months for the second year, and thereafter every 6 to 12 months for 2 or 3 years, and must have at least one negative spinal fluid examination at the end of the first year of observation. This is essential to guard against the possibility that the infection has been only suppressed, instead of eradicated, with the resultant likelihood of visceral, cardiovascular, or neurosyphilis in the future. If the patient is unwilling to subscribe to all of the above, especially the probationary follow-up, it is far better to withhold prophylactic arsphenamine and to observe him closely for the appearance of lesions or the development of a positive blood serologic test before treatment. (See subsequent paragraph "The Serologic Follow-up.")

Mechanical Prophylaxis

Since neither chemical nor chemotherapeutic prophylaxis is at present suitable for widespread application in practice, the main hope of prevention of syphilis and other venereal diseases is mechanical prophylaxis, the con-

dom. This is a method which is simple, painless, inexpensive, affords protection against all of the venereal diseases and to both sexes at once, and which, applicable before and during the act of intercourse, eliminates the psychologic hazards associated with the other methods. Its chief drawbacks at present are the poor quality of some of the condoms available on the market, the refusal of some types of individuals to use them, the ignorance of others as to their effective use, and the possibility of infection with syphilis on areas not covered by the condom.

In the interest of prevention of venereal disease, physicians generally should lend support to efforts to improve methods of manufacture and distribution of condoms, and should foster dissemination of information concerning their use. If every illicit sexual contact were protected by this means, venereal disease would immediately diminish.

THE PART OF DIAGNOSIS AND TREATMENT IN THE SYPHILIS CONTROL PROGRAM

For various reasons, however, chiefly ignorance and carelessness, neither the condom nor any other method of prophylaxis is likely to prove of major importance. A more certain method, well within the power of the medical profession and already successful in Scandinavia and Great Britain, lies ready at hand in *the prevention of spread of infection by means of the early and adequate treatment of every infected person.* The following simple facts cannot be too often repeated.

1. Syphilis is transmitted by direct or close indirect contact of infected and noninfected persons, or from the infected mother to her unborn child.

2. For the acquired disease, the danger of transmission of syphilis is practically limited to the first 5 years after infection, more particularly to the first 2 years, and especially to the periods at which actual moist lesions of mucous membranes are present. For the congenital disease, an infected mother may transmit syphilis to her child *in utero* at any time after her own infection.

3. The infectious lesions of syphilis are often insignificant, trivial, sometimes completely undetectable. In pregnant syphilitic women, such lesions are usually entirely absent.

4. Since infectiousness is practically limited to the early years of the disease or during pregnancy, control efforts should be centered on early syphilis (against the acquired infection) and on pregnant women (against the congenital infection).

5. Since the lesions of early syphilis are so often trivial or easily confused with other diseases, and since lesions are usually absent in the pregnant syphilitic woman, the clinical recognition of these two types of infection is extremely difficult for the average physician.

6. Fortunately, this clinical difficulty is overcome by the existence of a serologic test which is 95 percent efficient in recognizing untreated syphilis at any stage of its existence.

7. When infectious syphilis is recognized, infectiousness may usually be abolished within a few hours by a single injection of an arsphenamine, and the danger of contact transmission to others thus minimized.

8. However, a single injection of arsphenamine does not suffice to maintain the noninfectious state. Further treatment must be given, in combination with a heavy metal, to a minimum total of 40 weeks. This treatment must be continuous.

* * *

The plan of medical attack on syphilis is based on these eight points, which resolve themselves into two major steps:

1. *Find infected persons with early syphilis, and pregnant syphilitic women, and bring them under treatment.*

2. *Keep them under treatment long enough to accomplish permanent noninfectiousness.*

These two steps cannot, however, be accomplished without the cooperation of every physician in the country.

* * *

THE IMPORTANCE OF LATE SYPHILIS IN THE CONTROL PROGRAM

Though the major efforts of public health authorities must be centered on early syphilis, and on syphilis in pregnancy, late syphilis cannot be neglected. Infectiousness for others is still possible, even if not probable, for many years after the disease is acquired. Incapacity or death may result unless late syphilis also is treated, and individual and family suffering and economic loss to the community therefrom are enormous.

The clinical diagnosis of late syphilis is even more difficult than that of early syphilis for the average physician for two reasons:

1. All infected persons go through a period, varying in duration from a few months to many years, during which absolutely no symptoms or physical signs of disease are present; indeed, symptoms and signs may never develop. This is latent syphilis.

2. Late syphilis, although it attacks chiefly skin, bones, cardiovascular and central nervous systems, may involve any organ in the body. Like early syphilis it tends to mimic other diseases and diagnostic differentiation is often clinically impossible.

Here again, however, the recognition of untreated latent and late syphilis is simplified by the serologic test, which, as in early syphilis, is 95 percent efficient. For the recognition and bringing under treatment of all possible

persons with latent and late syphilis, the cooperation of every physician is again essential.

THE ROLE OF EVERY PHYSICIAN IN DIAGNOSIS

THERE are three reasons why every physician should interest himself in and cooperate with the syphilis control program:

1. There is a great deal of syphilis. Each year in the United States there are approximately 500,000 fresh infections; it is estimated that about 10,000,000 people in this country have or have had syphilis.

2. Syphilis is no respecter of persons, of social class, occupation, education, or financial status. While it is true that among Negroes and among whites in the lowest educational and income groups the incidence of infection is highest, no group is exempt. Infection usually occurs in youth or in early adult life.

3. In all stages of the disease early or late, syphilis tends to mimic other diseases. Few patients consult a physician complaining of syphilis. Their complaints are as diversified as human complaints can be: "Sores", skin eruptions, headache, eye trouble, deafness, stomach trouble, constipation, urinary difficulties, shortness of breath, weakness, neurasthenia, convulsions, vague pains and aches, and many others.

Thus no physician who sees patients, no matter what his specialty, can fail to number syphilitics among his clients. Most often, perhaps, they first consult the family physician or the general practitioner; but also they go direct or are referred to the ophthalmologist, otolaryngologist, urologist, gynecologist, obstetrician, pediatrician, neurologist, psychiatrist, orthopedist, gastro-enterologist, cardiologist, dermatologist, internist, and surgeon. All these general and special groups have an obligatory duty to perform in stamping out syphilis. This duty lies in the recognition of the prevalence of syphilis and a willingness to consider it as a diagnostic possibility—the maintenance of a "high index of suspicion", the recognition of the extent to which syphilis can imitate or be imitated by other diseases and the fallibility of clinical diagnosis, and the willingness to check clinical suspicion by the performance of the serologic test.

Diagnosis versus case-finding.—Since at any given moment, more than one-third of the syphilitic patients are in the stage of latency, and are clinically unrecognizable, the "high index of suspicion" toward patients actually consulting physicians is not enough to detect and bring under treatment all possible patients. Deliberate efforts at case-finding among those not actually ill are essential. These efforts must take four distinct forms, in which again the cooperation of all physicians is essential. These are:

1. The routine serologic testing of every pregnant woman as early as possible in pregnancy. Only in this way can congenital syphilis be eliminated.

2. The epidemiologic investigation of every patient with early syphilis.

3. The routine serologic testing of all members of the immediate family—wife, husband, children—of every patient with syphilis, early or late,

4. The routine serologic testing of as many patients as possible, no matter what their complaints, especially in hospital in-patient and out-patient services, but also in private practice.

These methods of case finding will presently be discussed in more detail

THE SEROLOGIC TEST FOR SYPHILIS

THE original serologic test for syphilis was a complement fixation test. known as the Wassermann test. Since its discovery in 1907, numerous modifications have been introduced, usually known by the names of the developers, e. g., the Kolmer modification. More recently a number of flocculation or precipitation tests have been developed, also known by name, e. g., in this country, the Kahn, Kline, Hinton, and Eagle tests. All these tests depend on the same fundamental physicochemical phenomena. While the several flocculation tests are simpler to perform than the complement fixation tests, they are more difficult to interpret and *none is suitable for performance by a technician or physician without special training.*

It is unnecessary for the physician to know the technical details of these tests. He should, however, be thoroughly familiar with the requirements of a satisfactory laboratory, with the interpretation of the terms used in reporting, and with the accomplishments of the particular test employed by the laboratory available to him.

A satisfactory serologic test must combine two factors—maximum specificity and maximum sensitivity. By the former is meant that the test shall give no false positive results in nonsyphilitic persons (in actual practice less than 1 percent false positive reports is satisfactory in this respect). By the latter is meant that the test shall give the largest possible proportion of positive results in patients with known syphilitic infection (in actual practice a satisfactory test will provide from 80 to 90 percent positive results in a group of untreated and treated syphilitic patients).[2] In order to furnish such results, a laboratory must constantly check its results by (a) intralaboratory check using two or more technics; (b) interlaboratory checks, in which one laboratory checks against another laboratory known to be reliable; and (c), most important of all, check of serologic results against known clinical diagnoses, preferably in a good syphilis clinic. Unless these three checks are provided, the laboratory is not satisfactory and should not be employed. Every physician should make it his duty to verify the use of these systems of checking in the laboratory of his choice.

[2] American Serologic Conferences.

Only three terms should be used in reporting serologic tests to the practitioner—positive, doubtful, and negative. The present current vogue of reporting in terms of + marks, e. g., ±, +, ++, +++, or + + + +, should be abandoned as misleading. The laboratory cannot make a diagnosis, but can only report objective findings to be interpreted by the clinician. The terms positive, doubtful, negative, have the following laboratory significance:

Positive =complete fixation of complement, e. g., in the Wassermann test or one of its modifications, or complete flocculation or precipitation, e. g., in the several flocculation tests.

Doubtful=incomplete fixation of complement or incomplete flocculation (of any degree).

Negative=no fixation of complement or no flocculation.

To the clinician, these terms have the following significance:

Positive.—Means syphilis, excluding the possibility of technical or biologic error, or of the presence of certain other diseases, mostly tropical. With the better tests (see below) positive results will be secured in from 90 to 95 percent of all patients with *untreated* syphilis, no matter what the stage of infection (excepting only primary syphilis within the first few days, see also below, p. 13). The tropical diseases frequently causing positive serologic tests are yaws, relapsing fever, and leprosy (50 to 100 percent positive) and less frequently malaria (5 to 10 percent positive). Other diseases and physiologic conditions, e. g., menstruation, pregnancy, do not usually cause false positive tests.

In the absence of definite history or physical evidence of syphilis, a single unsupported serologic test from any laboratory should not be accepted as evidence of syphilis. In order to guard against possible technical or biologic false positives (about 1 percent with the best of available tests), the unexpected positive test must be repeated in the same and preferably also in a different laboratory before the result can be accepted as evidence of syphilis. Occasionally, extended serologic study with a variety of different technics may be necessary to decide the validity of such a result.

Doubtful.—This result cannot be interpreted without full clinical data, and from the serologic standpoint signifies only an unsatisfactory test which should be repeated. It may mean syphilis, e. g., in the primary stage before the test has become completely positive, or in any stage as a result of reduction in the strength of the test by means of treatment. On the other hand, it may more frequently mean technical error than the false positive result, especially with the flocculation tests. Unless syphilis is definitely known to exist clinically, a doubtful result cannot be interpreted without further serologic study, and the report should there-

fore be qualified by the laboratory with words "Indeterminate—repeat!"

Negative.—Although a positive test, properly controlled, means that the patient has syphilis, a negative test does not necessarily mean that he is free from it. The negative result is strong presumption of the absence of syphilis, but it must be remembered (a) that no test so far developed is sufficiently sensitive to detect all patients with syphilis even if untreated, and that from 5 to 10 percent of patients with actual syphilitic disease, especially late, will have negative blood tests; (b) that the test may be negative as a result of previous antisyphilitic treatment; or (c) that in the first 10 to 14 days after the appearance of a primary lesion the test is usually negative, the diagnosis hinging on dark-field examination or serologic follow-up. The value of a negative serologic test in completely excluding the diagnosis of syphilis with certainty is precisely zero. Among the commonest errors of medical practice are the treatment of primary syphilis as chancroid, of cutaneous gumma as cancer or tuberculosis, of syphilitic osteomyelitis as pyogenic or tuberculous, of tabes dorsalis as "neuritis" because the serologic test was negative.

The Use of Multiple Tests

While multiple testing, e. g., a complement fixation test with several antigens, a complement fixation test checked by a flocculation test, several different flocculation tests, is desirable for intralaboratory check, the results are necessarily often conflicting because of the varying sensitivities of the several tests. These conflicts and discrepant results should not be reported to the practitioner, since he is rarely in position to interpret them correctly. It is much safer to report as follows:

(1) When all tests are positive="Positive."

(2) When the more sensitive tests are positive, less sensitive doubtful="Positive."

(3) When more sensitive tests are positive, others negative="Doubtful."

(4) When any test is doubtful, others negative="Doubtful."

(5) When all tests are negative="Negative."

In general, the desirable report is that of the test which combines maximum sensitivity with maximum specificity, disregarding other results of less sensitive or less specific tests.

The Most Satisfactory Present-Day Tests

The best of the commonly employed present-day tests should give less than 1 percent false positive results and from 70 to 80 percent positive results with known syphilitic patients. Various tests may be more sensitive, but this added sensitivity is often gained at the expense of lost speci-

ficity, i. e., while more positives are obtained in known syphilitics, so are more false positives obtained in nonsyphilitics. Any practitioner using laboratories which employ these more sensitive tests should be fully aware of their limitations and of the danger of diagnosing syphilis when it is not present.

The Responsibility of the Physician in Serologic Testing

Most of the present-day serologic tests require a specimen of several cubic centimeters of blood, which can be obtained only by venipuncture. If it is true, as has been estimated, that half of the physicians in the United States are unable to perform deftly the simple procedure of inserting a needle into a vein to obtain blood, the syphilis control program is seriously handicapped. Either all physicians should familiarize themselves with the technic of this procedure or simpler serologic methods must be developed. It may be possible to secure the widespread adoption by health department laboratories of a microprecipitation test (Kline, Eagle, Hinton), demanding only the collection of a drop or two of blood in a capillary tube from puncture of an ear lobe or a finger. Until such methods are more widely available than at present, however, venipuncture must be relied upon. *Every physician, no matter what his specialty, should know how to carry out this simple measure.*

THE DIAGNOSIS OF PRIMARY SYPHILIS

Importance of Early Diagnosis

The best method of preventing the spread of syphilitic infection is the prompt and adequate treatment of early syphilis. The patient himself may be spared the disastrous sequelae of late syphilis if his infection is properly managed at the beginning. Paradoxically, the best method of treatment of paresis, tabes, cardiovascular, and visceral syphilis is not the treatment of these conditions but their prevention by means of the thorough treatment of early syphilis. It is hardly too much to say that, given a cooperative patient, the development of late syphilis is the direct responsibility of the physician who treated the patient first.

The phrase "early treatment" needs still further definition. With cooperation on the part of the patient, it is possible to "cure" almost 100 percent of patients with seronegative primary syphilis, when the chancre is, on the average, of less than 14 days duration. By the time the patient with primary syphilis has developed a positive blood serologic test or the lesions of secondary syphilis, "cure" is possible under the best of treatment in only

about 80 percent. This means literally that a few days delay in starting treatment may mean the difference between "cure" and "no cure."

It is obvious, therefore, that all efforts ought to be toward speed and accuracy in the diagnosis of primary syphilis.

The diagnosis of primary syphilis is a laboratory procedure. The textbook descriptions of the clinical characteristics of chancre, as compared with chancroid, herpes, scabies, etc., are valueless in general practice. The primary lesion of syphilis may be a tiny abrasion, a ragged, dirty, painful, nonindurated ulcer, or a typical Hunterian chancre. The diagnosis cannot be made with certainty by looking at it or feeling it.

Every genital sore, in the male or in the female, and every extragenital sore which fails to heal promptly, should be regarded as possibly syphilitic until it can be proved to be otherwise.

The Comparative Value of the Dark Field and of the Blood Serologic Test in the Diagnosis of Primary Syphilis

When the chancre is less than 10 days old, the dark field is 90 to 95 percent efficient, while at this same time the blood serologic test is usually negative (about 40 percent positive). Up to the fifth week, about 80 percent of untreated primary sores may be identified with the dark field. Thereafter, the percentage of positive dark-field examinations in undoubted chancres declines rapidly, while the percentage of positive serologic tests rises, so that by the sixth week the serologic test is almost always positive.

No genital lesion should receive any local treatment until at least five consecutive daily dark-field examinations have been found to be negative, or until it has been otherwise identified as syphilitic (not as nonsyphilitic). This simple rule is more often violated than any other equally important medical principle. Antiseptics, especially mercurials, render the finding of Treponema pallidum difficult or impossible for a time. If any such application has been made to a suspected lesion, its use should be discontinued, the lesion thoroughly cleaned with soap and water, and followed with several hot normal saline soaks practiced for 24 hours before repeating the dark-field examination.

Since few physicians possess dark-field apparatus or are experienced in its use, the only safe rule to follow is that every patient (male or female) with a genital sore of any duration of appearance, or any patient with an extragenital sore (lip, finger, etc.) which fails to heal or is not readily identifiable within 10 days, *should be referred at once for dark-field examination to the nearest available laboratory, the patient reporting in person.* If no laboratory is available in the immediate vicinity, a specimen should be prepared by the following technic and forwarded by special delivery mail.

If the lesion is covered with a crust or scab, remove it. Then wash the lesion thoroughly with a gauze sponge wet with plain tap water (no soap) or with normal salt solution, to remove gross surface infection. This should be dried off, and the surface of the lesion abraded with a dry gauze sponge, sufficient to provoke slight bleeding and exudation of serum. As oozing occurs, gently wipe away the first few drops, especially if they contain much blood, waiting for a drop or two of clear serum to appear. Gentle squeezing is permissible. It is desirable to obtain serum from the depth, not the surface of the lesion. One or several drops of clear serum should be aspirated into a capillary tube (outfits supplied by many State health departments), the ends sealed with the wax compound supplied with the kit (not with heat), and mailed at once, special delivery (air mail if necessary) to the nearest health department laboratory, a telegraphic report being requested.

If the dark-field from the surface of the sore is negative, or if the lesion is completely epithelialized, one may aspirate the base of the lesion or a neighboring lymph node. For this is required a sterile Record or tightly fitting Luer syringe fitted with a stout needle of at least 20 gage. A drop or two of sterile normal salt solution is drawn into the syringe. The overlying skin is painted with iodine and alcohol and the node (or indurated base of the lesion) steadied between thumb and finger of the left hand. The needle is inserted well into the node, penetration of the capsule being indicated by the ability to move the node with the needle. The drop of salt solution is injected into the body of the node, the needle is manipulated in various directions to macerate the tissue about its point, and the injected salt solution and tissue juice aspirated. A drop of this is placed on a clean slip and slide, and examined at once for T. pallidum, or aspirated into a capillary tube as described above and forwarded at once to the nearest laboratory.

The presence of T. pallidum in lymph from a suspected lesion makes a positive diagnosis of syphilis. Failure to find the organism does not mean that the lesion is not syphilitic, and dark-field examinations should be made on at least five consecutive days before the search is abandoned.

The Serologic Follow-up

Every genital lesion is to be regarded as syphilitic until proved not to be. Even if repeated dark-field examinations are negative and the clinical characteristics of the lesion are those of chancroid, repeated blood serologic tests should be performed at intervals of 1 week for 1 month, and then every 2 weeks until 3 months have elapsed. The prevalence of mixed infections is such that about 15 percent of lesions clinically nonsyphilitic will subsequently prove to be syphilis.

The Therapeutic Test for Primary Syphilis

It is common for a physician, confronted with a suspicious lesion which is nevertheless dark-field and serologic-test negative, to feel that the diagnosis will be aided by response of the lesion to an injection of arsphenamine. *This practice is indefensible. The therapeutic test, of so much value in the diagnosis*

of some of the obscure late lesions of syphilis, should never be employed in suspected but not proved early syphilis. Nonsyphilitic genital lesions are prone to heal spontaneously, sometimes with great rapidity. If this healing is coincident with a diagnostic injection of arsphenamine, the physician is in the unfortunate position of not knowing whether or not the patient has syphilis, and is under the painful necessity of treating him as if he has. The modern intensive treatment of syphilis is such that this is not a light matter.

In suspected early syphilis, never start treatment until the suspicion is proved, unless you intend to carry through treatment to the end and exactly as if you were sure of the diagnosis.

THE DIAGNOSIS OF SECONDARY SYPHILIS

For all physicians except the expert, and often even for him, the diagnosis of secondary syphilis is also a laboratory procedure. There are no less than 38 skin diseases, 22 diseases involving the buccal mucous membranes, 14 diseases of the genital mucous membranes, 16 diseases of bones and joints, and 7 ocular diseases which early syphilis may resemble. The only safe rules for the general practitioner are as follows:

1. Any lesion which was possibly primary syphilis, i. e., any genital lesion in male or female, any indolent extragenital lesion, may be followed by secondary syphilis. *Do a 3-month serologic follow-up.*
2. Any generalized skin eruption, no matter what its appearance, may be secondary syphilis. *Do a serologic test.*
3. Any sore mouth or throat which does not heal in 10 days, no matter what its appearance, may be secondary syphilis. *Do a serologic test.*
4. Any unexplained patchy loss of hair may be secondary syphilis. *Do a serologic test.*
5. Any iritis may be secondary syphilis. *Do a serologic test.*
6. Any polyarticular arthralgia—"acute, subacute, or chronic infectious arthritis"—may be secondary syphilis. *Do a serologic test.*

Fortunately the blood serologic test has its greatest value at the time of the secondary outbreak. It is safe to say that in the presence of a generalized skin rash, a negative serologic test from a competent laboratory makes the diagnosis of secondary syphilis highly improbable. However, if in doubt, have the test repeated. One should not be satisfied with one negative result or with a "one plus" or a "two plus" report in such a doubtful case.

THE DIAGNOSIS OF LATENT SYPHILIS

Every physician must remember that all syphilitic infections are latent at some time in their course, and in most instances, after the healing of early

syphilis, are latent most of the time. *Latent syphilis is not clinically recognizable.* It can only be identified by routine serologic testing. Do routine serologic tests whenever possible.

THE DIAGNOSIS OF SYPHILIS IN PREGNANCY

What has been said as to latent syphilis is especially true of the disease during pregnancy. The lesions of syphilis are suppressed by pregnancy, and in 9 cases out of 10 syphilis in the pregnant woman is not clinically recognizable. Congenital syphilis can be prevented only if every doctor will do routine serologic tests on every pregnant woman as early as possible in pregnancy. If done, and found negative before the fifth month, the test should be repeated at the seventh month to guard against the possibility of infection late in pregnancy.

THE DIAGNOSIS OF LATE SYPHILIS

The difficulty of clinical diagnosis in early syphilis is multiplied a hundredfold in late syphilis. It is too much to expect of the average physician that he shall be a competent dermatologist (27 skin diseases may imitate late cutaneous syphilis), roentgenologist or orthopedist (33 diseases may mimic late syphilis of bones or joints), internist (21 diseases may be mistaken for hepatic syphilis, for example), ophthalmologist (13 diseases must be differentiated from late ocular syphilis), cardiologist (7 diseases to be separated including such nearly physiologic processes as arteriosclerosis), and neurologist (46 diseases may cause confusion).

The 147 diseases tabulated (but for lack of space not enumerated) are only those which commonly cause diagnostic difficulty, and not all the rarer conditions are included. The only way out of this diagnostic dilemma is, as previously suggested:

(a) A realization that there may be confusion between syphilis and other diseases, a willingness to consider syphilis as a diagnostic possibility, a "high index of suspicion."

(b) Free use of the serologic test. If this were done whenever the possibility of syphilis exists, and equally when it is not especially suggested, i. e., as examination routine, 90 to 95 percent of all cases would be properly diagnosed, and only 5 to 10 percent missed.

Examination of the Patient

An essential feature of the management of syphilis, early or late, is thorough study of the patient. At the first visit, accurate notes of important general data in the history (as well as a detailed history of syphilis) are recorded, and a complete physical and neurologic examination is made.

In every case of syphilis, inquiry should be made as to familial or other contacts who may have the disease and an effort made to secure their examination in order to discover and bring additional cases under treatment. In cases of early syphilis, the source of infection should be ascertained and brought under treatment whenever possible.

No physician should undertake the treatment of a case of syphilis unless he is willing to make and record the results of a careful physical examination of the patient. Nine-tenths of all the slipshod work on syphilitics occurs because the physician examines only the presenting lesion. Complete examination frequently reveals unsuspected lesions of syphilis, or coexisting disease such as tuberculosis, rheumatic heart disease, or nephritis which may play an important role in the patient's reaction to syphilitic infection or in his response to treatment. From the standpoint of the accurate study of syphilis, this thorough preliminary study and careful record of results provides information for comparison with subsequent examinations and for the evaluation of treatment.

To anticipate for a moment the question of the criteria of "cure," it should be said that no patient should ever be discharged from observation as "cured." If he is regular in treatment, he should be submitted to a complete physical examination every year or two. If he lapses from observation for several months, examination should be repeated as a routine before recommencing treatment. The interpretation of abnormalities discovered at these subsequent examinations would be impossible if definite statements regarding pupils, reflexes, lymph nodes, cardiac measurements, blood pressure, urine, etc., were lacking from the record of the first visit.

SOURCE OF INFECTION AND CONTACT EXAMINATION [3]

The duty of the physician to his patient and to the community does not end when he has established the diagnosis of syphilis and has undertaken the responsibility of therapy. He must consider two questions of fundamental public health importance: from whom did the patient acquire syphilis, and to whom may he have transmitted the infection? In solving these problems each stage of syphilis has different implications.

In order to perform successful syphilis epidemiologic work, the first step is to obtain the complete confidence of the patient. The private physician holds a strategic position in furthering this aspect of the syphilis control movement in that here the patient-physician relationship and support is ordinarily much stronger and more intimate than may be expected from the average clinic or public health organization. An intimate knowledge of the family and its social relationships, often an open book to the private

[3] The following paragraphs on case-finding and case-holding were written by Norman H. Ingraham, M. D., and Louise B. Ingraham, Philadelphia.

practitioner, makes easy a visualization of the problems involved and furnishes the advantageous setting required for obtaining usable epidemiologic information concerning contacts, always a delicate procedure.

Instruction of the patient.—After a preliminary discussion with each patient regarding the nature of his diseases, the method of its spread, the danger of late relapse, and the necessity of its "cure," he should be made to understand clearly why it is necessary that he be requested to expose the details of his personal conduct, of his sexual experiences and partners. He must know that his contacts may not experience warning symptoms such as his which indicate the need for medical care; that inadvertently tragedy may follow his failure to share his knowledge and his warning with them. Resentment against his supposed infector may be reduced to a minimum by showing him that he voluntarily risked infection and that the individual from whom he has acquired his infection is likely as blameless as he is in willfully spreading the disease. In the case of marital partners the question of infidelity presents a complication of more serious nature, but tactfully handled, it is by no means insurmountable. The promiscuous husband can often seek safety in admitting premarital exposure which has brought syphilis unsuspectingly into a marriage of fidelity. Others must find means of inducing wives or husbands to be examined through various ruses when overt confession seems impossible.

The contact is best approached through the informed original patient, and only when this means fails should other methods be resorted to or the health authorities called in. But the patient, usually lacking imagination, must be fortified by his physician with some simple way of expressing his mission when approaching his contact so that embarrassment may be minimized. When a faithful wife is the original patient with syphilis, a complete discussion of the diagnosis may be postponed until her consort has had an opportunity to clear himself or to work out some means of maintaining harmonious family relations in spite of damaging evidence of infidelity. Where family complications have already been precipitated, the offender will often take refuge in protests of fidelity. In these cases, a discussion of the facts of the case, time, and growing confidence may later result in confession and identification of extramarital exposure.

A simple means of obtaining medical care must be provided the patient in every instance, for him to present to his contact. If it is undesirable or impossible for the contact to be examined by the original physician the name of the examining physician should be secured and the results of the examination confirmed. Where absolute secrecy is demanded by the patient, contact examination can often be arranged by confidential communication between the patient's physician and the contact's physician, without other outside intervention of any sort.

If the patient is unwilling to approach his contacts but will identify

them for examination, a confidential investigator of the State or local health department, where such is available, may be called in by the physician for conference. The physician should be at liberty to instruct the investigator as to the type of approach he desires, guided in each instance by the type of problem in hand.

It should be remembered that in contact examination, it is usually not the action which antagonizes the community or its individuals, but the demeanor, attitude, or approach that is employed when examination of a potentially infected individual is required. It is a wise policy to secure, whenever possible, the consent of the patient before employing outside agencies.

Family investigation.—In the case of latent and late syphilis, the examination of the husband or wife should be undertaken whenever indicated through sexual history. Delay in the accomplishment of these examinations need not be discouraging, since a time interval has already elapsed before the original patient came under treatment. Withholding the diagnosis may again prove charitable providing regular treatment can be maintained.

The children of syphilitic parents should always be examined when indicated, as determined from the relation of their birth to the onset of the disease in the parent when this is obtainable.

Pregnant syphilitic women should always be impressed with the importance of (1) postnatal supervision of their expected infants, (2) continuation of their own treatment postpartum, and (3) the necessity for treatment during subsequent pregnancies and the medical supervision of future children.

Printed instructions for the patient furnished free of charge by many States and municipal boards of health or upon request by the United States Public Health Service, Washington, D. C., are valuable in supplementing the physician's personal instructions.

Case-holding.—A careful initial instruction of the patient, already alluded to, will tend to minimize his tendency to disappear from observation before completion of treatment, especially if the duration of observation essential to "clinical cure" and the likelihood of minor treatment reactions are clearly understood from the start.

It seems absurd that communications from physician to patient designed to further the patient's welfare should ever be interpreted as solicitation. Personal letters or communications, relative to the resumption of treatment, to the lapsing syphilitic patient are the duty of the physician if he properly fulfills his responsibility to the public health and to humanity.

Resources of highly trained public health workers, now available in many States, may be freely utilized in the follow-up of the syphilis patient in private practice without conscientious objection. When the activities and

attitude of this personnel is not known by the physicians, personal conference with them is certainly indicated. They will usually be found competent to further the confidential relationship between the patient and the physician and, in following lapsed patients, to act with finished discretion for the best interest of all concerned.

THE TREATMENT OF SYPHILIS

The Role of Every Physician in the Treatment of Syphilis

In general, physicians may be divided into three groups, so far as the treatment of syphilis is concerned:

(1) A group which, lacking knowledge of the fundamental technical procedures of venipuncture, intramuscular injection, lumbar puncture, asepsis, and the preparation of drugs, should not attempt to treat the disease at all. Such physicians are under a positive obligation to refer all syphilitic patients to a more experienced colleague or to a clinic. The technical procedures involved are of such a nature as to require practical experience; they cannot be learned from texts or figures.

(2) A group able to perform these procedures, but lacking detailed knowledge of choice of drugs, reactions, clinical and serologic response of patients, etc. This group may and should treat patients with syphilis subject to the following qualifications:

(a) All patients with early or latent syphilis may be treated, provided the physician adheres rigidly to standard outlines of treatment prepared for such patients on the basis of massive clinical experience. (See pp. 52 and 58 of this article.)

(b) Some patients with late syphilis requiring (as most do) highly individualized treatment procedures or schedules, provided expert guidance is sought and accepted. Patients with serious treatment reactions should also be handled in the same manner.

(3) Expert syphilologists capable of handling any treatment situation. Such physicians—all too few in number—have a threefold function to perform for colleagues and patients, as follows:

(a) To diagnose and treat all patients referred to them for these purposes.

(b) To carry out special treatment procedures too complicated or too dangerous for general use, e. g., fever therapy, subdural treatment, etc.

(c) To serve as periodic consultants to the practitioner in planning treatment for complicated cases (practically all patients with late syphilis, those with treatment reactions), to check the results of treatment at periodic intervals (usually of 6 to 12 months), and to plan for further treatment or observation if necessary. Under these circumstances, the practitioner acts as the consultant's agent in carrying out treatment.

The Economic Aspect of the Treatment of Syphilis

It is desirable to explain to the patient at the start that he is faced with a long continued and, under any circumstances, relatively expensive treatment. Some idea should be given him of what the treatment may be expected to cost. If he cannot pay for the basic arsphenamine and bismuth treatment necessary to "cure" him, it is absolutely unjustifiable to jeopardize his chance of "cure" by giving him poor or worthless treatment at the price he can afford. In this case he should be referred to a clinic.

One must remember that syphilis is usually contracted in youth when earning capacity is small; that the patient, through his own or his physician's fault, often fails to obtain adequate early treatment because of his inability to pay the fee demanded; and that 10 or 15 years later, when his income has increased to a point which makes it possible for him to obtain good treatment, his infection has perhaps produced hopeless lesions of the nervous system or cardiovascular apparatus for which no amount of money can buy a "cure."

The Local Treatment of the Early Lesions of Syphilis

Aside from ordinary cleanliness, no local treatment of uncomplicated syphilitic lesions is necessary. Excision of the chancre is valueless, and should not be attempted. The local application of antiseptics or mercurials is unnecessary in lesions not secondarily infected, as the disappearance of surface treponemes and healing of the lesion is prompt under arsphenamine.

The Systematic Treatment of Early Syphilis

A routine plan of treatment, which might be strictly adhered to by the relatively inexperienced practitioner though modified at will by the expert, is desirable in early syphilis as opposed to late syphilis, where extreme individualization of treatment is often necessary. There is now general agreement as to the best scheme of treatment for early syphilis though differences of opinion between specialists may occur on minor points. This article will present a treatment outline which has proved satisfactory in practice and as to the essential points of which there is general agreement among the members of the committee of experts appointed by the Public Health Service.

A routine plan of treatment applicable to all patients with uncomplicated early syphilis is desirable for three important reasons. For the most part, early syphilitics are healthy young adults free from the extensive anatomic involvement of important viscera so frequent in late syphilis, and free from the degenerative and sclerotic diseases of advancing years. At this stage of the infection, also, there is more uniformity in the character of the

lesions and in the distribution of treponemes in the tissues, than is the case with the varied localizations and lesions of late syphilis. Finally, both clinical and experimental evidence indicate that radical "cure," in the sense of eradication of the last treponeme, is attainable in early syphilis but questionable after the disease has existed a year or more and the organisms have become firmly intrenched in the tissues.

THE ARSPHENAMINES

The Cooperative Clinical Group studies have demonstrated the superiority of arsphenamine (606) to neoarsphenamine (914) in early syphilis (16 percent more satisfactory results, 4 percent less clinical relapse). It is in use in most large American syphilis clinics. However, its proper neutralization with alkali makes its preparation so difficult for the unskilled practitioner that he is usually unwilling to undertake it. Excessive or insufficient neutralization may provoke reactions. This fact, together with the greater amount of time necessary for its administration (large bulk of fluid, gravity method) has led to the much more widespread use of the simpler neoarsphenamine. Nevertheless, arsphenamine remains the arsenical drug of choice in early syphilis.

Neoarsphenamine is therapeutically less active than arsphenamine, and if employed in early syphilis should be used in correspondingly larger doses and in longer courses. Roughly, for each 0.1 gram of arsphenamine, a corresponding dose of 0.2 gram of neoarsphenamine should be used. Moreover, neoarsphenamine as furnished in the market is more apt to vary in toxicity and in therapeutic effect than arsphenamine. Low toxicity with corresponding excellent tolerance by the patient does not necessarily mean that the product is of the maximum degree of efficiency.

Mapharsen is a new product recently introduced. Chemically it is arsenoxide, the therapeutically active break-down product of all other arsphenamines. Experimentally, it is 10 times as toxic as arsphenamine, and is used in correspondingly smaller doses (0.04 to 0.06 gram in place of the 0.3 to 0.6 gram dose of arsphenamine). Mapharsen is still in the experimental stage, and its final value in the treatment of early syphilis will not be determined for some years. Early studies indicate, however, that it is at least equal to and possibly the superior of neoarsphenamine, as regards the disappearance time of surface organisms, healing of lesions, and serologic reversal in early syphilis; and that it produces distinctly fewer mild and serious reactions than any other of the arsphenamines.

Silverarsphenamine may occasionally be used in early syphilis if avoidance of "ether odor" and mild reactions is desired. Argyria may follow its long and continued use.

Sulfarsphenamine has no place in the treatment of adults because of

its tendency to produce serious reactions. Infants and young children tolerate it well.

Tryparsamide is useful only in neurosyphilis.

Acetarsone (stovarsol) has been recommended for oral administration in the treatment of syphilis, especially congenital syphilis. It is still in a highly experimental phase, and is not advised.

Other arsenical drugs than those mentioned should not be employed by the inexperienced physician.

The dosage, advantages, and disadvantages of the drugs named are given in the following table.

ARSPHENAMINE

Dosage	Advantage	Disadvantages
Average, 0.3 gram, women; 0.4 gram, men. For first attack in early syphilis (3 doses), 0.3 gram to 0.6 gram (0.1 gram per 25 pounds body weight). A course equals 6 to 8 doses.	Therapeutic superiority to other products in average dosage. Best in early syphilis. Results achievable in early syphilis definitely known. Most stable arsphenamine product. Best adapted to mass treatment (clinic). Uniform toxicity and therapeutic effect. Cheapest arsphenamine.	Technical difficulty of administration (alkalinization, gravity method, large volume of fluid, poor veins). Slightly more prone to produce mild gastro-intestinal reactions than others. Tendency to thrombose veins; less desirable in fat patients, poor veins, infants. Inadvisable in cardiovascular syphilis.

NEOARSPHENAMINE

Average, 0.6 to 0.75, women; 0.75 to 0.9, men. For practical purposes, best to assume that 8 to 12 doses 0.9 gram neo equals 6 to 8 doses 0.4 gram arsphenamine. In weak or debilitated patients, 0.2 to 0.6 gram. In cardiovascular syphilis, 0.1 to 0.45 gram. A course equals 6 to 12 doses.	Good in cardiovascular syphilis (in dosage of 0.2 to 0.45 gram). Low toxicity from small doses; fewer gastrointestinal reactions. Marked tonic effects. For weak, debilitated, cachectic, very young and very old patients. Less irritant to veins (no thrombosis). Easy to give (no alkalinization, syringe method, small needle usable in poor veins).	Lower therapeutic efficiency than arsphenamine in doses often used. Results achievable not as good as with arsphenamine. Batches of drug from different manufacturers, or even from same manufacturer, may vary in therapeutic efficiency. Unstable product, deterioration possible in ampule. Also unstable in solution. Slight errors in technic markedly increase toxicity (shaking, standing). Larger number injections required than arsphenamine. Relatively high incidence immediate reactions ("ether" odor, nitritoid crisis). More expensive than arsphenamine.

MAPHARSEN

Dosage	Advantage	Disadvantages
Average, 0.04 to 0.06 gram, men or women. In cardiovascular syphilis 0.01 to 0.02 gram, increasing gradually and cautiously to 0.03 to 0.04 gm.. A course equals 6 to 12 doses.	Simple to give. Low toxicity, few reactions, mild or severe. Immediate therapeutic effect equal to or better than neoarsphenamine.	Ultimate results in early syphilis not yet definitely known. Still in experimental stage. More expensive than arsphenamine.

SILVERARSPHENAMINE

0.1 to 0.3 gram, women; 0.1 to 0.4 gram, men. A course equals 8 to 10 doses.	Probably equal to neoarsphenamine in therapeutic value in doses ordinarily used. Much less likely to produce immediate (nitritoid) or slightly delayed gastro-intestinal reactions. No odor. Patients intolerant to other arsphenamines may take it. Not irritant to veins; no thrombosis. Some clinical experience indicates that it may be of most value in neurosyphilis. Easy to give (no alkalinization, syringe method).	Technically difficult of administration because of black color of solution (column of blood aspirated into syringe difficult to see). Unsettled clinical status. Exact definition of ultimate results obtainable not yet settled.

SULFARSPHENAMINE

Must be used intramuscularly, never intravenously. Should never be used in adults. For infants, 10 to 25 milligrams per kilogram body weight. For infants, a course equals 6 to 8 doses.	The only arsphenamine well tolerated intramuscularly. Best for early congenital syphilis (infants). Stable in ampule and solution. Few immediate reactions. Easy to give.	In adults, alarmingly high incidence of serious reactions (dermatitis, nephritis, blood dyscrasias)—so high that it should not be used unless unable to give one of the other arsphenamine products intravenously. Infants seem less susceptible to these reactions. Unsettled clinical status.

TRYPARSAMIDE

1 to 3 grams, average 3 grams. A course equals 12 to 24 doses.	Valuable in neurosyphilis (especially early paresis) before or after malaria. Marked tonic effect. Easy to give (directly soluble, syringe method). Few reactions (except visual damage). Usable in patients who have had arsphenamine dermatitis.	No value in any type of syphilis except central nervous system involvement. Prone to produce visual damage. Not usable in patients with preexisting optic-nerve injury.

The special indications for the use of these several preparations are provided in the following table.

Type of Syphilitic Infection

Drug	Early acquired	Early congenital	Latent	Late	Cardio-vascular	Neuro-syphilis	Late congenital
Arsphenamine.	Yes; always when possible.	No.	No.	No.	Never.	Yes.	No.
Neoarsphenamine.	Yes; with compensatory dosage increase.	No.	Yes.	Yes.	Yes; small doses.	Rarely.	Yes.
Mapharsen.	Yes.	No.	Yes.	Yes.	Yes.	Status unsettled.	Yes.
Silver-arsphenamine.	Rarely.	No.	Rarely.	Rarely.	Rarely.	Yes.	Yes; especially for interstitial keratitis.
Sulfarsphenamine.	Never.	Yes.	Never.	Never.	Never.	Never.	Never.
Tryparsamide.	Never.	Never.	Never.	Never.	Never.	Yes.	Never.

PREPARATION AND TECHNIC OF ADMINISTRATION OF THE ARSPHENAMINES [4]

ARSPHENAMINE

Materials Required

A. Erlenmeyer flasks, 250 to 1,000 cc capacity.
B. Funnels, glass, 4-inch.
C. Cylinders, graduated, 100 to 500 cc capacity.
D. Gravity apparatus, consisting of—

1. Gravity graduated glass cylinders, 300 cc capacity, graduations for each 5 cc.
2. Rubber tubing, pure gum, heavy wall, inside diameter $\frac{5}{32}$ inch (about 4 mm), of lengths to limit height of the cylinder to 3 feet above the patient's arm.

Caution.—Before being used the first time the tubing should be filled with 4 percent sodium hydroxide solution for not less than 6 hours. It should then be thoroughly rinsed in water, sterilized by boiling, and then thoroughly rinsed with sterile water again just before using.

[4] The material of the following section is largely abstracted and slightly modified from Reprint No. 774 from the Public Health Reports, "Preparation and Administration of Arsphenamine and Neoarsphenamine. Standard Instructions for the Preparation and Intravenous Administration of Arsphenamine and Neoarsphenamine for Use by the Medical Departments of the Army, of the Navy, and of the Veterans' Bureau, and by the Public Health Service," issued July 1, 1922.

3. Needles (preferably stainless steel) with slip joint, 19 or 20 standard gauge, medium bevel. The correct gauge is highly important, as it influences the rate of flow. Proper care of the needles is important. They should be cleansed immediately after use. Just before sterilization, the point should be freshened on a stone, if necessary. A dull needle tends to make a dissatisfied patient, damages the vein, and leads to infiltration.

4. Glass tubing, 6 mm in diameter, for windows, which should be inserted in the rubber tubing a few inches above the lower end.

5. Adapters for attaching needles to end of tubing. These may be of metal or glass. If of glass they will serve as extra windows as well as adapters.

6. Pinchcocks (Mohr's) for cutting off the flow, to be applied a short distance above the needle.

E. Sterile gauze, cut in small squares, for filtering the solution.

F. Sterile freshly distilled water. This water should be sterilized by autoclaving or boiling in Erlenmeyer flasks, stoppered with a gauze or cotton plug.

G. Sterile normal (0.85 percent) salt solution, made with water prepared as above and chemically pure sodium chloride. Sterilization should be carried out as described above. The use of salt solution in the place of distilled water for the dilution reduces the danger of producing thrombophlebitis and also reduces the danger of producing reactions.

H. *Sodium hydroxide solution (4 percent).*—Enough of this can be prepared at one time to last for a month or longer, provided it is kept in a rubber stoppered wax- or paraffin-lined bottle. There is danger of deterioration on account of absorption of CO_2 from the air and of reactions with the glass container. A wax-lined bottle can be prepared by placing wax or paraffin in a bottle, sterilizing with dry heat, and spreading the melted wax by rotation over the inside of the bottle as it is cooling. If precipitate is found in the alkali, it is probably an evidence of deterioration of the solution, which should be discarded. For use in large clinics, a 2-liter bottle protected from the action of the alkali and of the atmospheric CO_2 and set up with an automatic measuring burette is a great convenience and will insure the safe-keeping of the alkali for a long period.

I. *Burette or pipette.*—A graduated burette or pipette for accurately measuring the alkali.

All the glassware mentioned above should be of chemical standard. All apparatus should be surgically clean, freshly sterilized, and cool at time of using. The apparatus should be sterilized by dry heat or autoclave, with the exception of the tubing and the needles, which should be boiled.

Inspection of Drug

A. Note and record name of drug, manufacturer, lot number, and particularly the dosage stated on the label. *Be sure to read the label carefully before use.* Fatal accidents have occurred, even in experienced hands, by neglect of this precaution. It is convenient and economical to employ dosages which are just sufficient to make up the unit batch of solution desired, e. g., if 10 doses of 0.4 gram are made up at a time, use ampules containing 4 grams. An ampule containing 10 doses is the largest that should be used.

B. Examine ampules critically and do not use any which are cracked or in which the powder is not freely mobile and is not of a pale yellow to a lemon yellow in color. Forward any suspected ampules with explanatory letter directly to the National Institute of Health, Washington, D. C., for examination.

C. The ampules, having satisfactorily passed preliminary inspection, should be immersed in 95 percent alcohol, primarily to detect any minute cracks in the glass not

visible on preliminary inspection and also to cleanse the ampule. Lay ampules on sterile towel to dry, or wipe off alcohol with sterile gauze.

Preparation of Solutions

A. The amount to be prepared at one time will depend on the number of patients, but unit batches of more than 10 average doses should not be prepared.

B. Place in a sterile Erlenmeyer flask about 10 cc of freshly distilled sterile water for each decigram of arsphenamine to be used, e. g., 100 cc for 1 gram. Open ampule and sprinkle—do not dump—contents on surface of water. The flask should not be shaken because of aeration and increased toxicity, but solution may be facilitated by a rotary swinging motion. When the arsphenamine has completely dissolved, forming a perfectly clear solution with an absence of any gelatinous particles when viewed by transmitted light, it is ready for alkalinization. If for any reason the arsphenamine fails to form a perfect solution it must be discarded, but it must be remembered that if alkali is added before solution is perfect, clouding will always result.

C. Correct alkalinization is extremely important; failure to alkalinize properly causes more reactions than any other error connected with the use of arsphenamine.

1. The exact method consists in the addition all at once of 0.85 cc 4 percent sodium hydroxide solution for each 0.1 g of arsphenamine used; e. g., 8.5 cc for 1 g of drug. This is the correct amount necessary to form the disodium salt of arsphenamine, the form which is best tolerated by the patient.

2. Approximate method of alkalinization. An exception may be made to the rule that only standardized 4 percent alkali solution should be used, in case this solution is not obtainable. Under such circumstances, the exact concentration of alkali in solution being unknown, the operator should add the solution drop by drop. With the first few drops, a precipitate forms which promptly is redissolved. This changes acid arsphenamine to the monohydrochloride, which is still highly toxic and must not be injected. When a little more than one-fourth of the amount of the alkali indicated in the above paragraph has been added, the precipitate no longer redissolves. From this point on, until almost three-fourths of the amount of alkali necessary to form the disodium salt has been added, the precipitate remains and does not redissolve on shaking. But when three-fourths of the total amount necessary has been added, the precipitate redissolves. It is at this point, when just enough alkali has been added to dissolve the precipitate, that the solution has very frequently been injected. This solution of the monosodium salt is the most frequent cause of reactions. At this point only 75 percent of the correct amount of sodium hydroxide solution has been added, hence an amount equal to one-third of the total alkali solution used up to this point should be added.

The P_H of a proper solution is about 10, and it is impossible to buffer it to neutrality with common buffers without precipitation. Moreover, the alkaline solution is well tolerated if given slowly and well diluted. Over-alkalinization causes pain along the vein during injection and subsequent thrombosis.

D. Filtration and dilution to proper strength of the alkalinized solution. With sterile forceps place 4 layers of sterile gauze in the funnel. Wash with sterile water. Pour alkalinized solution of arsphenamine through this gauze into a graduated cylinder and then rinse the filter with enough cold sterile saline solution to bring the total for each decigram of drug up to 20 cc, e. g., for 1 g of arsphenamine 200 cc of solution should be made. This washing of the drug through the filter insures full dosage.

E. Time the solution should be allowed to stand.—The properly alkalinized filtered and diluted solution should now stand for at least 30 minutes before being injected, to allow completion of the chemical reactions. The toxicity is considerably reduced by

this delay. The solution may stand as long as 3 hours without undergoing any increase in toxicity, provided it is protected from the air, not shaken, and provided the temperature does not exceed 30° C. The solution is now ready for administration.

Administration

A. Emphasis should be laid on a complete physical examination of the patient preliminary to administering arsenical treatment, for evidence of renal, cardiovascular, or visceral changes, in the presence of which it should be used cautiously. Frequent urinalyses should be made during treatment. The patient should be questioned concerning any reactions following the last treatment, with special reference to itching or any toxic skin eruptions as danger signals against further treatment. Any evidence of an exfoliative dermatitis is an absolute contraindication against any further treatment with a trivalent arsenical. Evidence of jaundice should also be looked for and, if present, should be taken as an indication for caution. In late cases the possibility of a Herxheimer reaction following a large injection should be remembered. This may be fatal should vital structures be involved. Each patient should receive individual consideration.

B. Preparation of patient.—The patient should be given a mild cathartic the night before and should eat no food within 2 or 3 hours before the injection. Only a light meal should be taken within a few hours following the injection. If large doses are being given, the patient preferably should be kept in bed until the following morning.

C. The patient should be placed in a recumbent position.

D. The gravity apparatus should be arranged to provide a column of solution not over 3 feet in height. The tubing should be rinsed with sterile water, then the cylinder and tubing should be filled with the solution and the air expelled by lowering the end of the tube below the level of the fluid in the cylinder. Apply pinch cock.

E. Select a suitable vein in either arm and sterilize the overlying skin by applying tincture of iodine, which should be removed after a minute or two with 95 percent alcohol.

F. Apply rubber tourniquet.

G. Insert needle, bevel up, in two stages (first through the skin, second into the vein), and allow a few drops of blood to escape to indicate the entrance to the vein. The needle should be slid well into the vein in order to avoid escape of the point from the vein on further slight manipulation. Now connect adapter attached to gravity apparatus. Open pinch cock and snap it over the window in the tube.

H. Rate of injection.—If the specifications as to the gauge of needle, etc., have been followed, the correct rate of injection is practically insured, i. e., by the size of the needle and the length of the tube; however, this should not be taken for granted, but the exact time should be observed, and in no case should the rate exceed 20 cc in 1 minute or an 0.4 gram dose in 4 minutes; 5 minutes is preferable. The rate of flow should be even as well as slow. Should the patient show any signs of an immediate reaction, stop. It is highly desirable, in sensitive patients, to wait a minute or two after injection of the first 0.1 gram before proceeding with the rest of the injection. When the necessary amount has been injected, cut off the flow with the pinch cock, disconnect the tubing, allow a few drops of blood to escape; then withdraw the needle and place sterile gauze over the puncture, instructing the patient to hold the gauze there for a few minutes. If another injection is to be given and there is any suspicion of contamination of the tubing with blood, empty the cylinder and start over with a new sterile tube.

NEOARSPHENAMINE

The administration of neoarsphenamine is much simpler than that of arsphenamine. Neoarsphenamine is readily soluble in a small quantity of water, and must not be alkalinized. It may be given by the syringe method.

Apparatus Required

1. Sterilize freshly distilled water.
2. 10 to 50 cc all-glass syringes.
3. Needles, 25 standard gauge, medium bevel.
4. Sterile medicine glasses, for mixing drug.

Inspection of Drug

Caution—Read the label.—(Do not mistake arsphenamine for neoarsphenamine.) An even more critical examination should be made than in case of arsphenamine, as neoarsphenamine occasionally decomposes in the ampule, even when no cracks are present. A greater danger is that of mistaking arsphenamine for neoarsphenamine, and such a mistake usually means death to the patient. Note and record name of product, maker, lot number, and dosage. The powder should be freely mobile and lemon yellow to canary yellow in color. When it approaches a red color, or is distinctly lumpy or solidified, do not use it, but forward samples to the National Institute of Health for examination.

Immerse in alcohol the ampules which have passed inspection, for the further detection of the presence of cracks and to clean the ampule.

Preparation of Solution

A. Amount to be prepared at one time.—In marked contrast to the practice with arsphenamine, do not prepare any more solution at one time than can be administered within 20 minutes.

B. Concentration.—The concentration preferably should be 1 decigram to 5 cc of water. Concentrations as high as 1 decigram in 0.5 cc of water may be used under special circumstances. The highly concentrated solutions, however, should be given very slowly.

C. Solution.—

1. Put in a sterile Erlenmeyer flask or medicine glass 5 cc of sterile distilled water for each decigram of neoarsphenamine. If necessary a concentrated solution can be made in the ampule itself by using sterile distilled water supplied in another ampule. (Caution: The distilled water must be at room temperature not to exceed 30° C.)

2. Open the ampule and sprinkle—do not dump—the powder into the water and, by preference, allow it to go into solution with no agitation whatever. Slight rotation of the flask is permissible. Shaking the solution increases its toxicity and should be avoided.

In case the solution is not perfectly clear and transparent under no circumstances should it be used. Whether it requires 1 minute or 10 minutes for the drug to form a perfect solution is unimportant, but it should not require more than 10 minutes. The important point is not the rate of solubility but the complete solubility of the drug.

3. As soon as the neoarsphenamine is in solution, add an equal volume of water or normal salt solution, making the concentration of drug 1 decigram in 10 cc. The solution is now ready to inject, and, in marked contrast to the arsphenamine solution, which should stand at least 30 minutes before the injection, the neoarsphenamine solution should be injected immediately. In no case should it be allowed to stand longer than 20 minutes.

The directions given for arsphenamine apply to the administration of neoarsphenamine, with the exception of the dosage, rate, and method of injection.

Rate: The injection must be given slowly. In no case should more than 0.1 gram of neoarsphenamine be injected in 30 seconds, or 0.6 gram in 3 minutes. Special care must be taken to carry out this rule.

MAPHARSEN [5]

The administration of mapharsen is as simple as that of neoarsphenamine. It is likewise readily soluble, must not be alkalinized, and may be administered by syringe.

Apparatus Required

1. Sterilize freshly distilled water.
2. 10 to 50 cc all-glass syringes.
3. Needles, 21 standard gauge, medium bevel, 1¼″ long.
4. Sterile medicine glasses, for mixing drug.

Inspection of Drug

Read the label for dosage. Since mapharsen is a white powder, it cannot be confused with the yellow arsphenamine and neoarsphenamine. *Do not use the drug* if it is discolored brown or black. Inspect the ampule for cracks.

Preparation of Solution

A. Amount to be prepared at one time.—This drug is relatively stable and as much solution may be prepared as can be given in one hour.

B. Concentration.—Concentrated solutions are desirable. Not more than 10 cc of water should be used for a dose of 0.06 gram.

C. Solution.—Place 5 to 10 cc of sterile distilled water in a sterile medicine glass or flask, and dust the powder on the surface. Solution is rapid, and agitation, shaking, or "squirting" is advisable to aerate the solution thoroughly.

Administration

As for neoarsphenamine except for the rate of injection, which *should be rapid* (10 seconds or less for a dose of 0.06 gram). This drug does not cause nitritoid reactions, but slow injection and insufficient aeration may cause intolerable pain along the course of the vein which can be obviated by rapid *injection and thorough mixing*.

SILVERARSPHENAMINE

Method of Injection

Silverarsphenamine may be injected by either the gravity or the syringe method. All injections of silverarsphenamine should be made intravenously. When the syringe method is employed special care must be taken to inject slowly.

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[5] Any new arsenical drug advocated for use in the treatment of syphilis, if it is to be accepted as an equal of the arsphenamines, must meet the following requirements: (1) It must be as actively spirocheticidal as the arsphenamines and possess the property of healing open lesions as quickly as do the latter preparations: (2) It should prevent the communicable forms of relapse with the same degree of efficiency; (3) It should prevent the late crippling manifestations of syphilis to the same extent as do the arsphenamines. Mapharsen has been proven to be effective as far as the first two requirements are concerned. Only time can demonstrate its efficacy in the prevention of the late crippling manifestations of the disease.

Injection of Drug

A critical inspection of the drug should be made in the case of silverarsphenamine because of its incompatability with carbon dioxide and the carbonates. The powder should be of a dark-brown color and freely mobile in the ampule. Any powder which is distinctly lumpy or solidified should be sent to the National Institute of Health for inspection. Immerse the ampules which have passed inspection in alcohol to reveal further the presence of cracks and to cleanse the ampule.

Preparation of Solution

A. The amount prepared should not exceed that which can be used in a half hour. The presence of carbon dioxide in the air will tend to decompose these solutions.

B. Concentration.—For use in the gravity method 1 decigram of the drug should be dissolved in 5 cc of cold, sterile, freshly distilled water, and then be diluted with 5 cc of sterile saline or water. Injections should require 3 to 4 minutes. When the syringe method is used a full dose of 0.3 g or less may be dissolved in 10 cc of distilled water and then diluted with an equal volume of saline solution. The temperature of the solutions should be that of the ordinary room.

C. Solution.—Open the ampule and sprinkle—do not dump—the powder into the water and, by preference, allow it to go into solution with no agitation whatever. Slight rotation of the flask is permissible. Shaking the solution increases its toxicity and should be avoided.

In case the solution is not perfectly clear and transparent, under no circumstances should it be used. Whether it requires 1 minute or 10 minutes for the drug to form a perfect solution is unimportant, but it should not require more than 10 minutes. The important point is not the rate of solubility, but the complete solubility of the drug.

It is desirable, though not essential, to filter the solution through sterile gauze, and it may be allowed to stand as long as 20 minutes before injection.

Administration

Inject slowly and evenly. This can best be done by the gravity method. If the syringe method is used, be particularly careful about the rate, allowing 3 to 4 minutes for the injection.

SULFARSPHENAMINE

Method of Injection

Sulfarsphenamine should never be given intravenously. It is less effective when given by this route than when given intramuscularly, and the incidence of reactions is higher. It is the preparation of choice in infants and young children. In adults it should never be used unless intravenous medication is difficult or impossible.

Inspection of Drug

The most important part of the inspection is to note the amount contained. Serious results have followed the administration of excessive doses, many physicians believing, because of the low toxicity of the drug to animals, that patients can tolerate large doses. This has not proved to be the case. In infants the dose should be accurately measured at 15 to 25 mg per kg of body weight. In adults, an average dose is 0.4 g; 0.6 g should

never be given. The powder should be of a light yellow cast and be freely mobile. The ampule should be immersed in alcohol to clean it and to aid in discovering cracks.

Preparation of Solution

A. For intramuscular injections, select an ampule containing the proper dosage, open, and with a 2 cc syringe, add 0.3 cc of cool distilled water for each decigram of drug, which should dissolve quickly and completely. This highly concentrated solution appears to be tolerated better than more dilute solutions. Aspirate into the syringe and inject intramuscularly (see technic of intramuscular injections). If for any reason the above dosage is exceeded, it is preferable to divide the dose between the two buttocks.

B. Caution.—Batches of sulfarsphenamine have been encountered which in concentrated solution soon formed a jell, and if injected in this condition intravenously probably would have caused serious or fatal accidents. Hence the highly concentrated solutions mentioned above for intramuscular injection should never be used for intravenous injection.

C. Dosage.—The average maximal dose should be 0.4 g for the average adult and should not be given oftener than every 5 to 7 days, with not more than 12 injections in a course.

TRYPARSAMIDE

This preparation is a pentavalent arsenical compound which has proved to be of great value in the treatment of syphilis of the central nervous system, particularly early general paralysis. *It should not be used in cases of syphilis without involvement of the central nervous system.* The only serious reaction to be feared from the use of this drug is visual damage. It may affect the optic nerve, producing partial or complete atrophy. Tryparsamide should not be used in patients with preexisting visual damage, and any patient in whom it is proposed to use the drug must first be examined by a competent ophthalmologist as to the state of the fundi, visual acuity, and especially the visual fields, before treatment is begun. At the slightest complaint of visual difficulty during treatment this special examination must be repeated, and if there is constriction of the visual fields, tryparsamide must be discontinued.

The drug is an easily soluble white powder. The maximum dose of 3 grams may be dissolved in 20 cc of sterile, freshly distilled water and administered by the syringe method. Treatments should never be given oftener than once a week.

REACTIONS FOLLOWING INJECTION OF THE ARSPHENAMINES

If the methods of administration and dosage described above are followed, serious reactions should be relatively rare. If a serious reaction does occur, a complete report should be forwarded to the Surgeon General of the Public Health Service, giving the clinical history, dose injected, lot number, and name of the manufacturer. Samples of the same lot of drug should also be sent if possible. Most important of all, some of the solution injected, when any remains, should be forwarded for examination.

In spite of all precautions, however, mild reactions frequently, and more serious ones occasionally occur. These vary in severity from slight undefined passing distress to symptoms of grave poisoning. These reactions may

be due to individual hypersensitiveness to the drug, to pathologic changes in the body (both of syphilitic and nonsyphilitic origin), or to the drug itself or the method of administration.

Reactions may be divided for consideration into three classes—immediate, slightly delayed, and late—i. e., the early reactions occurring during or immediately after injection, the slightly delayed from 6 to 24 hours after, and the late occurring from 1 day to several weeks after administration of the drug. The common and more important reactions will be described. Reference to certain rare reactions will be found in standard texts.

IMMEDIATE REACTIONS

1. Severe burning pain usually associated with an obvious lump at the site of injection is due to extravasation of the drug into the tissues about the vein resulting from faulty technic. Infiltration of the tissues with any of the arsphenamines produces a disabling and very painful induration which lasts for days or weeks, and may slough. If infiltration is apparent, the needle should be withdrawn immediately and a different vein chosen for injection. The pain of infiltration may be minimized by hot applications. The local injection of sodium thiosulfate is useless.

2. Aching pain in the arm and shoulder during injection is, with arsphenamine, usually due to faulty alkalinization, and is apt to be followed by thrombophlebitis. With mapharsen, the cause is unknown but is apparently due to too slow injection, or to insufficient aeration in mixing. With this drug, it may usually be obviated by very rapid injection.

3. The patient often complains during the injection of an annoying odor, usually of "ether." This is most common with neoarsphenamine and arsphenamine, and is not a feature with the other products discussed. It may be avoided by having the patient hold his nose and breathe through his mouth, or by having him inhale the fumes of aromatic spirits of ammonia or chew a fresh piece of gum.

4. The nitritoid crisis, mild or severe, is characterized first by a sense of cutaneous flushing, injection of the conjunctivae, choking, cough, palpitation, and vomiting (especially if treatment is given on a full stomach), and more rarely by edema of the lips, tongue, glottis or face, syncope, and thready pulse. It may be accompanied by very severe cramplike pain in the lower back (lumbar muscles?). It is probably due to a variety of causes, of which the most important is too rapid administration of the drug. Other causes are insufficient alkali in mixing of arsphenamine, idiosyncrasy on the part of the patient, or impurities in the drug. It rarely follows the first injection of the drug. If it occurs once, it is likely to be troublesome with subsequent injections. It is especially common after arsphenamine and neoarsphenamine (frequency perhaps 2 to 5 percent of all injections),

quite rare after silverarsphenamine or sulfarsphenamine (the latter intramuscularly), and practically unknown after mapharsen or tryparsamide.

If this reaction is anticipated, it usually may be prevented by the subcutaneous or intramuscular administration 5 to 10 minutes before treatment of 0.5 to 1.0 cc of 1:1,000 adrenalin solution, or by the subcutaneous injection of 1.3 mg of atropine sulphate 20 minutes before treatment, or by injection of one-tenth of the total dose of the arsphenamine to be administered and waiting 1 hour before injecting the other nine-tenths. It is often most convenient to change the arsenical preparation used, e. g., from neoarsphenamine to mapharsen or arsphenamine.

5. Sudden syncope, greenish pallor, rapid cardiac failure, and death sometimes immediately follow the administration of large doses of the arsphenamines, especially arsphenamine itself (606), to patients with cardiovascular syphilis. Individuals with this form of syphilis should receive preparatory treatment for 2 to 3 months with iodides and heavy metal, following which they may be given neoarsphenamine in small doses (not more than 0.3 gm) or mapharsen (0.02 to 0.04 gm) in preference to other arsenical preparations.

6. Excruciating pain in the back and chest, cough, collapse, pallor, cardiac failure, and usually death are due to the injection of concentrated solutions of unneutralized (acid) arsphenamine. Treatment of this unfortunate accident is difficult, owing to the fact that all the arsphenamine probably is precipitated in the lung capillaries, and the effect is that of massive pulmonary embolism. Warmth, circulatory stimulants, and oxygen inhalations may be tried.

7. Tubing reaction. If one is using a gravity apparatus with new rubber tubing which has not been previously soaked in sodium hydroxide solution, as advised above, a reaction may occur within an hour after injection characterized by chill, pain in the back and legs, excitement, fever to 102° or 103° F., vomiting and diarrhea, prostration, and herpes febrilis. This is due to removable impurities in new gum rubber and may be prevented by proper precautions. Treatment is symptomatic. Recovery may take 4 or 5 days.

SLIGHTLY DELAYED REACTIONS

1. The commonest form of reaction following the use of any of the arsphenamines appears 4 to 12 hours after treatment, and is characterized by malaise, headache, nausea, vomiting, and diarrhea. These symptoms commonly last a few hours only, but may be prolonged for several days. If short in duration and mild in intensity, they may be disregarded in subsequent treatment, but if the reaction is prolonged for a day or more, it may be an indication of growing intolerance, and further treatment should be administered cautiously.

Mild reactions of this type occur more frequently in women than in men

and more often after arsphenamine than neoarsphenamine. Perhaps 25 percent of all injections of an arsphenamine, under average clinic or office conditions, will result in this relatively negligible difficulty.

The reaction is due to a variety of causes such as impurities in the water employed, under-alkalinization, dietary indiscretions, or constipation, on the part of the patient, etc. Treatment is symptomatic.

2. A reaction similar to that described above may be accompanied by fever and a skin eruption which is usually urticarial, macular, or scarlatiniform. This is much more serious evidence of arsenical intoxication and calls for expert advice and the utmost caution in subsequent treatment.

LATE (DELAYED) REACTIONS

1. *Jaundice.*—The relationship of so-called postarsphenamine jaundice to treatment is not yet clear. Jaundice may appear from two days to several months after the last arsphenamine injection. Mild cases are clinically indistinguishable from acute catarrhal jaundice. There is usually a gastro-intestinal upset, often with nausea and vomiting, which lasts several days. As this subsides, jaundice appears, with bile in the urine and clay-colored stools. The jaundice may persist for several weeks, during which time, except for mild lassitude, the patient may feel quite well. Examination frequently reveals an enlarged and tender liver but nothing else of interest. One may encounter all stages of severity in this reaction, from the mildest indisposition to a rapidly progressive and fatal acute yellow atrophy of the liver. The frequency of mild jaundice is, according to the Cooperative Clinical Group experience, 1 per 1,000 arsphenamine injections; of acute yellow atrophy, 1 per 50,000 injections.

Until more is known about this complication, all arsenical treatment should be suspended while evidence of liver damage is present. Jaundice is not a contraindication to further arsphenamine after complete recovery, but if the drug is used again, its use should be begun very cautiously (arsphenamine 0.05 g increasing by 0.1 g steps, etc.)

The reaction should be treated by light diet, elimination, forced fluids, saline catharsis, possibly duodenal drainage, and rest. Sodium thiosulfate is useless in the treatment of this reaction, but intravenous glucose (daily injections of 1,000 cc of 5-percent solution) and calcium gluconate (1.0 g in 10 cc of water) should be given until clearing of the jaundice is obvious. Severe cases should be hospitalized and carefully watched. These cases call for expert attention.

2. *Dermatitis.*—This reaction may vary from fleeting erythematous eruptions to a severe exfoliative dermatitis. Its occurrence is often heralded several weeks before the reaction itself actually appears by persistent and generalized itching. This symptom should serve as a danger signal and

calls for the prompt abandonment or modification of subsequent arsenical treatment, preferably under expert advice.

Certain types of dermatitis are mild reactions which need not interfere with subsequent treatment; others mean that the patient is permanently sensitized to the drug and that he should never receive another dose of it, no matter how small. In a discussion of this nature, perhaps the most that can be said is that if the eruption is vesicular (forms blisters), if it shows any tendency to scale or exfoliate, or if it is accompanied by marked itching, the idea of further arsphenamine treatment must be permanently abandoned. If there is any question which arises on this point, expert consultation should be requested.

One of the arsphenamine series, sulfarsphenamine, is many times more likely to produce dermatitis than other members of the group, and its use should be attended with particular caution.

Fortunately for many patients with syphilis of the central nervous system, tryparsamide does not produce dermatitis, and may be used subsequent to a severe arsphenamine dermatitis.

Dermatitis may, according to the Cooperative Clinical Group, be expected to occur about once in every 1,300 injections, no matter what precautions are taken. It must always be regarded as potentially serious—about 5 percent of the cases result fatally. No matter how mild the original attack may appear to be, further arsphenamine treatment, if given at all, must be carried out with the utmost caution and under constant expert supervision.

If the reaction is severe the patient should be hospitalized. Itching may be relieved by sterile olive oil rubs (if very severe, not to exceed 0.5 percent phenol may be added to the oil) or by the colloid bath. The utmost precautions must be taken to avoid skin infection from scratching, and also upper respiratory infections. These patients are unusually susceptible to infection. Sodium thiosulfate is useless and should not be employed. As with jaundice cases, the patient should be treated with daily intravenous glucose and calcium gluconate.

Standard texts should be consulted for further details.

3. *Renal damage.*—The arsphenamines may produce renal irritation, which is likely to be more marked if mercury or bismuth is used simultaneously. The urine should be examined before and frequently during treatment and should be specially watched in those patients known to have had previous renal involvement (coincident chronic nephritis is most frequent in late syphilis).

4. *Blood dyscrasias.*—Purpura and aplastic anemia are very rare and very serious arsphenamine accidents. They may be associated with arsenical stomatitis. Treatment with sodium thiosulfate is unsatisfactory. Repeated blood transfusions may prove helpful.

5. *Hemorrhagic encephalitis.*—This is one of the rarest (in this country) and most serious of arsphenamine reactions. It is characterized by early lethargy, difficulty in speaking, restlessness, muttering delirium, coma, convulsions, and may result in death. Its successful treatment depends on prompt recognition, repeated spinal drainage, repeated intravenous injections of 5 percent glucose solution, and repeated subcutaneous or intravenous injection of large doses (1 to 5 cc) of 1:1,000 adrenalin solution. (Caution as to intravenous injections!)

THE JARISCH-HERXHEIMER REACTION

This reaction consists in a flare-up of the lesions of syphilis after the first injection of an arsphenamine, as, for example, in secondary syphilis, with intensification of the skin rash or osteocopic pains 12 to 24 hours after treatment, together with malaise and fever. The reaction does not occur after immediately subsequent arsphenamine injections. It is of clinical importance in early or late syphilis, if there is a syphilitic lesion in a vital portion (liver, nervous system, cardiovascular apparatus, larynx, eye, or ear) of the body. Here, for example, one must be especially cautious in gummatous lesions of the larynx, in myocardial syphilis where there may be a lesion of a coronary artery, in aneurysm, and in cerebral vascular syphilis. The reaction may be avoided by starting treatment with a small dose of arsphenamine (0.1 g or its equivalent) or better still, in selected cases, by beginning treatment with a month or two of bismuth or mercury and potassium iodide.

VISUAL DAMAGE FROM TRYPARSAMIDE

As already pointed out, this drug should not be employed in patients with preexisting optic atrophy. In about 5 percent of patients with apparently normal eyes the complaint will arise (usually during the first 6 weeks of treatment) of blurred, dim, or smoky vision. Often the sensation is described as that of watching the hot air arise from an automobile radiator on a cold day. Sometimes the patient complains of flashes of light before his eyes (phosphenes). The occurrence of any of these symptoms calls for the immediate suspension of treatment and consultation with a competent ophthalmologist. Treatment should be resumed only under joint expert syphilologic and ophthalmologic supervision.

GENERAL CARE OF PATIENT

The specific drugs have a tonic effect on many patients, but not upon all. A rough gage of tolerance to treatment is the patient's weight, which should be carefully observed throughout. Marked loss of weight without

obvious cause calls for temporary suspension of treatment. It is essential that the spirits of the patient be kept up and that close attention be paid to the general state of health. A not too heavy but sufficiently nourishing diet should be prescribed.

Excesses in all things should be avoided, especially overwork, worry, alcohol, and tobacco. Plenty of sleep should be insisted upon.

BISMUTH VS. MERCURY

Except under unusual circumstances, early syphilis cannot be cured by the arsphenamines alone; it is necessary to combine them in some fashion with bismuth or mercury or both. It is even more unjustifiable to attempt to cure early syphilis with bismuth or mercury (or both) to the exclusion of the arsphenamines. Bismuth acts in much the same way as mercury, but is therapeutically more active (Cooperative Clinical Group data—12 percent more satisfactory results with arsphenamine and bismuth than with arsphenamine and mercury, and 6.5 percent fewer relapses). Also, dose for dose, bismuth is much less likely to produce toxic effects than the insoluble mercury salts. In most cases of syphilis, therefore, bismuth has completely replaced mercury, and the practitioner will rarely if ever, have occasion to use the latter.

Bismuth

Bismuth can be administered satisfactorily in only one way, i. e., by intramuscular injection. Other routes are either highly dangerous, completely valueless, or still in the nebulous experimental stage.

Mouth administration.—Has received much recent publicity, but is still in the completely experimental state. This route should not be used except by experts under strictly experimental conditions. Available evidence so far indicates that the method is relatively valueless as compared with intramuscular injection, and if utilizable at all, is certainly not so in early syphilis.

Intravenous administration.—Too dangerous for general use. Bismuth products are without exception from 10 to 100 times as toxic by the intravenous as by the intramuscular route.

Inunction.—Worthless.

The bismuth products available for treatment by *intramuscular injection* may be separated into four groups, of which the following are representative:

1. Water soluble—thioglycollate, tartrate.
2. Soluble in other vehicles—sodium iodobismuthate (in ethylene glycol).
3. Oil soluble—camphocarboxylate.
4. Insoluble in water, suspended in oil—subsalicylate, metallic bismuth.

The water soluble preparations are absorbed and excreted rapidly (24 to 48 hours), so that treatment is necessary every day or every other day.

Absorption of salts soluble in other vehicles (ethylene glycol, oil) is slower (3 to 4 days), and treatment need be given only twice a week, but these preparations are usually painful and much more expensive than insoluble salts.

With insoluble salts, especially the subsalicylate, absorption is slowest of all (may take 3 to 4 months for complete absorption of single dose), but with average therapeutic doses, cumulative toxic action need not be feared. Injections need be given only once a week (a marked advantage) and are relatively painless. This is the cheapest form of bismuth treatment available.

The practitioner is therefore, advised to limit himself to a single bismuth preparation, preferably the insoluble subsalicylate suspended in peanut oil or olive oil. The concentration of different manufacturers differs slightly, but is usually a 10 percent suspension. The dose is 0.2 g of subsalicylate (*not* 0.2 g metallic bismuth), at 5 to 7 day intervals. A course is 6 to not more than 12 injections.

Mercury

For the general practitioner the use of mercury is now rarely desirable. The chief indication is in alternation with bismuth in a patient permanently sensitized (dermatitis) against the arsphenamines. Very rarely mild oral mercury treatment may be given to elderly patients ("mixed" treatment, consisting of 1 to 2 teaspoonsful three times a day, of a mixture of mercury and potassium iodide [hydrarg. chlor. corros., grs. 1½; potassium iodide, drams 4; water, ounces 4]; or protoiodide pills, gr. ⅙ to ½ three times a day; or mercury with chalk grs. 1 three times day).

The best way of administering the drug is, however, by inunction, instructions for the exact carrying out of which are given herewith:

INSTRUCTIONS FOR THE PATIENT

The Rubbing Treatment

READ THESE INSTRUCTIONS CAREFULLY

This is the best method of administering mercury, but in order for the treatment to be successful, *it is absolutely* necessary: (1) *For you to understand* each step of the method, and (2) for you to be willing to devote time and energy to it. SUCCESS OR FAILURE DEPENDS ON YOU.

This ointment when rubbed on the surface of the body is

absorbed by the skin. The medicine contained in it is taken up by the blood and carried to all parts of the body.

DIRECTIONS FOR RUBBING

The best time to rub is before going to bed. *Take a hot bath beforehand*, or if a complete bath is impossible, wash well with soap and hot water the part to be rubbed that night.

When thoroughly dry, take out of the jar, on the end of a spoon or spatula, a *portion of ointment about the size of the end joint of your little finger* (as big as a large lima bean).[1] Spread a little of this portion on the skin and with the *flat palm of the hand* rub it in slowly and not too hard, putting on a little more ointment from time to time until the portion for that night has all been rubbed in. This ought to take *20 minutes* and you should *time yourself* by a clock.

Rub a different part of the skin every night of the week so that no part is rubbed more than once a week. The rubbing should be done over a *part of your skin four times as large as your hand.*

The best places to rub are—

First night.—Upper part of one thigh in front.
Second night.—Upper part of one thigh in back.
Third night.—Inner sides of both arms.
Fourth night.—One side between hip and armpit.
Fifth night.—Other side between hip and armpit.
Sixth night.—Upper part of other thigh in front.
Seventh night.—Upper part of other thigh in back.
Eighth night.—Start all over again.

Your back is a good place to rub if you have someone to do it for you. *Avoid rubbing very hairy areas* such as the armpits. If *pimples break out* in any of these places you are rubbing too hard.

If after 20 minutes' rubbing, any ointment seems to be unabsorbed, the excess may be wiped off the skin with a soft clean dry cloth, or if preferred, with a cloth soaked in a little benzine.

While taking this treatment *please report in person or by letter* (1) two weeks after starting the treatment, (2) once a month thereafter.

Stop the treatment and report at once if:

Your *teeth ache.*

Your *gums become swollen*, painful, inflamed or bleed easily.

You have *any persistent pain, diarrhea, or headache.*

[1] At least one manufacturer puts up a weighed 4-gram dose of Unguentum Hydrarg. in waxed paper. This is the easiest method of prescribing the drug.

There is now little reason for the practitioner ever to utilize the intravenous or intramuscular routes for the administration of mercury, and these should rarely be employed.

Toxic Effects of Bismuth and Mercury

The chief toxic symptoms produced by these two drugs are identical. In practice bismuth is considerably less prone to produce toxic symptoms than mercury. This is an added reason for its use. The most important sign of bismuth or mercury intoxication is renal irritation. In a patient under treatment with either of these drugs, the urine should be examined frequently for albumin and casts. The appearance of either in significant quantities is a signal for the suspension of this form of treatment.

Gastro-intestinal complications, chiefly enteritis and diarrhea, are more frequent from mercury than from bismuth.

Stomatitis and salivation, which is frequently a most disagreeable feature of the intramuscular use of the insoluble salts of mercury, is rare with the bismuth dosage suggested. A "bismuth line" is more common. This consists of a blackish blue line of pigmentation on the gums about the base of the teeth, sometimes also appearing as grayish blue areas about the fauces and soft palate. It is due to the deposition of metallic bismuth or bismuth sulfide in the tissues and is similar to the lead line found in lead poisoning, though without the graver significance of the latter. The bismuth line is not, in the absence of actual stomatitis, a contraindication to the further use of the drug. In the use of either mercury or bismuth the patient should be instructed to pay careful attention to oral hygiene. The removal of foci of infection in teeth is important. Every care should be taken to instruct the patient in maintaining scrupulous cleanliness of the teeth, and the use of an antiseptic astringent mouth wash should be prescribed. The excessive use of tobacco predisposes to stomatitis in a patient receiving mercury or bismuth. Before starting treatment with bismuth or mercury, the patient should visit his dentist for cleaning of the teeth and removal of tartar.

Technic of Intramuscular Injection

The buttocks are the most suitable muscle masses to utilize in the treatment of syphilis. Intramuscular injections should be given into the upper outer quadrant of the buttock. If given in the upper inner quadrant, one is likely to strike bone or to deposit the injected material near the roots of the sacral plexus, from which a troublesome sciatica may result. If given in either lower quadrant, there is pain on sitting, and there is more danger of striking the sciatic nerve or large vessels.

The only apparatus necessary is a 2 cc Luer all-glass syringe and 18 to 20

gage needles 1.5 to 2.5 inches long, depending on the fatness of the buttock to be injected. These instruments should be sterilized by boiling, not by alcohol. The syringe is filled with the substance to be injected before the needle is attached. If the drug to be injected is in suspension in a thick oil or fat, the syringe should be filled while hot so that the mass may be liquefied.

The patient lies face down on a long table, thoroughly relaxed, and with his feet "toed in." After preliminary sterilization of the skin with iodine and alcohol, the operator draws the buttock down with the left hand toward the patient's heel, to fix the tissues. The needle may be inserted separately or attached to the syringe. A separate insertion is preferable, since if a large vessel is accidentally struck, blood will flow from the needle. In either case, however, a deep insertion is made with a short, sharp stroke, the direction of the needle being slightly inward and downward from the vertical.

Even though no blood appears at the needle hub, aspiration should always be done as soon as the syringe is attached and before any material is injected. The injection of an insoluble salt (especially bismuth) in oil suspension into a vein is always accompanied by distressing symptoms of pulmonary oil embolism, and may result fatally. Arterial embolism may produce local gangrene of buttock and genitalia. If blood does flow from the needle or is obtained even in the smallest amount on the subsequent aspiration, the needle must be withdrawn and reinserted at least 1 cm or more from the original puncture.

As soon as it is apparent that no blood can be aspirated, the injection may be made. The suspension or solution should be followed by the injection of 1 cc of air to clean the needle and prevent leakage along the needle track. The needle is then rapidly withdrawn, and the site of the injection massaged vigorously and deeply for 2 or 3 minutes. The buttocks should be used alternately.

Painful superficial nodules or lumps are usually due to too shallow injection or leakage along the needle track and are best treated by local heat and massage. Large deep indurations may result from a too deep injection. With proper care for sterility, abscesses should not occur except with sulfarsphenamine. With this drug, especially in infants, a sterile abscess may occur about once in a thousand injections.

THE IODIDES

The use of potassium or sodium iodide in early syphilis is advisable largely on an empirical basis. If these drugs are of value in dissolving granulomatous tissue, they should enhance the penetrability of arsphenamine, bismuth, and mercury even in the comparatively slight lesions of early syphilis. The iodides are contraindicated in tuberculosis.

STANDARD TREATMENT PROCEDURE IN EARLY SYPHILIS

The following discussion is based on and in large part quoted from the work of the Cooperative Clinical Group.

Eligibility of Early Syphilis for Standardized Procedure

Treatment in late syphilis requires individualization, but attention to the individual is not so essential in the management of early syphilis. The management of early syphilis is amenable to a considerable degree of routinism, standardization, and mass technic, principles of which have so wide a degree of applicability that they can be formulated into definite rules and systems for all but universal use. The clear definition of the aims possible at the early stage of the disease, the youth and relatively good health of the patients, their freedom from the intrinsic damage produced in later life by years of syphilitic infection, all make standardization easy, acceptable, and a positive asset in the great aim of the ultimate extinction of the disease.

The Aims To Be Achieved

In late syphilis, the aim of treatment is preventive and symptomatically "curative" rather than radically "curative." The period of infectiousness and transmission over (except in the pregnant woman), "cure" in the sterilizing or complete sense is probably out of the question. In early syphilis, on the other hand, the evidence of the laboratory and the more slowly accumulated presumptions of clinical experience indicate that radical or complete "cure" is possible by an appropriate treatment technic, and infectiousness, limited largely to the primary, secondary, and relapse manifestations of the first 2 years and to the semen, becomes the crucial issue in public health control. The aims in early syphilis may, therefore, be defined as first, the prevention of transmission by treatment, and second, the individual "cure."

Syphilis, treated or untreated, is most infectious early in the course of the disease, grows less so with the lapse of time, and is rarely infectious (but may be so) after 5 years. Late acquired or congenital syphilis, with or without manifestations, is not infectious (except in pregnant women for their unborn children). Infectiousness has nothing to do with the serologic test; many infectious persons have negative tests, and conversely many with positive tests, e. g., in late syphilis, are not infectious. Infectiousness is controlled and syphilis will be eradicated only by treatment of the infectious person. The public health responsibility of the physician is, therefore, with the *early* months and years of the disease.

Treatment to control infectiousness must be continuous, not intermittent. Rest periods encourage relapse. The critical point for relapse lies between

5 and 9 injections. An equal number of doses of heavy metal are required as an adjunct to treatment. The minimum duration of treatment is, therefore, 40 weeks. For the sake of individual "cure" (see below) this should be prolonged to 15 or 18 months.

There is a relapsing type of early syphilis regarding which no rules or predictions can be formulated. In such cases, infectiousness may reappear immediately after or even during arsphenamine treatment (drug resistance). In such cases, the practitioner should seek expert consultation.

Infectiousness in syphilis is therefore a function of three factors: (1) time (the first 5 years of the disease, especially the first 2 years); (2) arsphenamine (a minimum of 20 injections, given in alternating courses with a heavy metal by the continuous method); and (3) individual predisposition to relapse.

The protection of others during the infectious period demands (a) treatment of the patient; (b) continence, or failing this, absolute mechanical protection of the sexual partner (condom, and 33-percent calomel ointment as lubricant); (c) avoidance of moist kissing.

Protection of the child of the pregnant syphilitic woman demands only treatment of the mother (see below).

The Individual "Cure"

The term "cure" must be used with circumspection and the use of quotation marks throughout this entire article expresses its status as a clinical presumption rather than as an established fact. There are no available absolute criteria of "cure" at this time, and many more years of observation will be required to establish its status. None the less, for practical purposes, "cure" is a complete extinction of all symptoms and signs of the disease, with nontransmission of the infection over a lifetime, or as close an approximation to it as present day follow-up of clinical material permits us to study. "Cure" as here used is, therefore, essentially:—that the patient has been followed for 2 years or more, and that during one probationary year he has had no symptoms of syphilis, his blood serologic test has been consistently negative, he has had a negative spinal fluid examination and a negative physical examination, or has had a reinfection.

Briefly expressed, among patients under observation and treatment for 2 years or more, the highest proportion of satisfactory results obtained under conditions stated in the next paragraph, was 71.4 percent under all methods of treatment taken in the aggregate, and 86.4 percent satisfactory results when treatment was "continuous" as distinguished from "intermittent", "intensive", and "irregular".

The "Golden Opportunity" reduced to figures.—The superior outlook of treatment begun in the primary stage of syphilis before the blood serologic tests become positive (seronegative primary) has been justified abundantly by

statistical analysis. The proportion of "cures" when treatment is begun in the seronegative primary stage (diagnosis by the dark field or other identification of *T. pallidum*) is given above, 71.4 percent average, and 83 to 86 percent best results. When, through failure of the patient to present himself or of his physician to diagnose primary syphilis until the blood test becomes positive, treatment is not begun until the so-called seropositive primary stage, "cure" is attained in only 53.3 percent by average and 64 to 70 percent by the best methods. This represents a clear loss of 18 percent in outlook for "cure" by the delay. If the patient goes on to the development of a secondary eruption, of course with a positive blood test, "cure" is attained in only 50 percent by average and 61 to 82 percent by best methods. This represents a possible loss of 21 percent by average and 14 percent by best methods, over the outlook prevailing when treatment is begun in the seronegative primary stage.

Duty to the individual patient, even more than duty to the public health, demands the earliest possible diagnosis, as well as the earliest possible application of treatment.

Combined Arsenical and Heavy Metal Treatment and Its Functions

It is accepted now as axiomatic that no patient with early syphilis should be treated by the sole use of an arsenical. To do so may lead to an unprotected state of high susceptibility to the most critical forms of relapse involving the nervous system (neurorecurrence), the liver, and other structures. In an unknown proportion of cases it does more—it directly predisposes the patient to an allergic reaction that forms the basis of so-called malignant precocious tertiarism—the development of highly destructive gummatous lesions within a few months of the primary stage. The protection of the patient from these dangers consists in the invariable use of mercury or bismuth in conjunction with arsenical therapy, either simultaneously (concurrently) or in alternating courses. Just as no patient should be treated exclusively with an arsenical, so also no patient should be treated exclusively with a heavy metal—even with bismuth, for all that it possesses greater spirocheticidal qualities than mercury. Its inferiority to the arsphenamines in this regard has been clearly demonstrated.

The Control of Relapse by Treatment

The general principles of this phase of treatment from the standpoint of infectiousness have been summarized. But it is worth while to emphasize further the existence of the relapsing type of patient, whose recurring infectiousness is a menace to the public health (12 percent of 3,244 patients). The figures supporting the statement that arsphenamine is absolutely necessary to the control of infectious relapse in the treatment of early syphilis are clearly defined; 35 percent of infectious relapsing patients had had less

than 5 arsphenamine injections and 81 percent had had less than 15 injections. Of those who had 20 or more injections only 2 percent ever sustained an infectious relapse. Thus 20 injections of an arsphenamine becomes the minimal optimal number needed in the individual patient to control the danger he represents to his contacts and to the public health.

It should be emphasized that in the first 6 months after treatment ceased, nearly one-half (45 percent) of the relapses had occurred; by the end of the first year 73.4 percent; by the end of the second year 91 percent. Hence the critical time of probation for the treated patient is the 2 years following the cessation of treatment, and no promises should be made, no precautions relaxed, and no observation neglected during this period. An increased rather than a diminished frequency of blood tests, and periodic inspection of the mucosae, skin, and anogenital region are essential during this probationary period. Especially should pregnancy and mechanically unprotected intercourse be even more strictly controlled after than during standard treatment in early syphilis.

The Danger of the Rest Interval or Lapse

One of the most important contributions of recent years to the technic of treatment of early syphilis has been to the question of intermittent as distinguished from continuous treatment. It may now be said with positiveness, that the old practice of administering treatment in early syphilis by fits and starts, conditioned on the report of the blood serologic test, is pernicious; that even the introduction of a few weeks of complete rest from treatment into the management of the first 18 months of the disease is likely to be profoundly injurious; that the patient who lapses or escapes treatment during this period is his own worst enemy; and that NO REST INTERVALS and a regimen in which the patient is *constantly receiving either an arsenical or a heavy metal during the first year* of the disease or longer if the indications require, is the best and safest modern practice both in the interest of the patient and of the public health.

The figures supporting these forcible and uncompromising statements are clear cut. They were obtained both by a study of infectious relapse and by the analysis of serologic and clinical results on the basis of four modes of treatment—the continuous, just described; the intermittent, in which rest intervals or complete breaks in treatment were introduced into the normal course whether purposefully or through the patient's negligence; the intensive, which involves a short (3 or 4 injections) course of arsphenamine alternating with a heavy metal course in units with long rest intervals between the arsenic-heavy-metal units; and finally, irregular treatment, totally irregular and uncontrolled, with long and short courses, and rest intervals in fortuitous disarrangement.

Continuous treatment, then, whether prolonged or brief and practically regardless of the drugs used, is superior in its results to the intermittent or other schemes of treatment. The continuous method secured the reversal of the blood serologic test by the end of a year in 81.8 percent, whereas the intermittent scheme of treatment with rest intervals of a month or more secured only 37.3 percent of reversals, and irregular treatment gave only 4.7 percent of serologic reversals within a year. It appears that in early syphilis, that great bugbear of physician and patient, the fixed or irreversible positive Wassermann reaction in treated early syphilis, lies at the door of the rest interval or lapse from treatment rather than in any peculiarity of discase or drugs.

In the matter of relapse, treatment continuously administered resulted in fewer relapses of all kinds than treatment with rest periods or lapses (continuous treatment 13.1 percent relapse and Wassermann-fastness, as against 20.8 percent with intermittent, 45.3 percent with irregular, and 41.5 percent with intensive treatment).

End results after 2 years show even more clearly the dangers of the rest period and irregularity of treatment as well as the inadequacy of the short arsphenamine course in the intensive system. With continuous treatment 79.7 percent achieved satisfactory or "curative" results, with intermittent treatment (rest intervals) 65 percent, with irregular treatment 33.3 percent, and with intensive treatment 23.4 percent.

Prolonged Treatment, Fixed Schedule, and "Abortive Cures"

It has become inexcusable to shorten treatment either because the patient was seen early in the course of the infection (seronegative primary syphilis), or because his blood test, originally positive, is reversed to negative within the first year. The former conception, that of so-called abortive cure, has been abandoned. The latter conception, much more widely prevalent in this country, also should be abandoned. *The serologic findings are an unsafe guide to the time of cessation of treatment.* The patient should usually not be informed of a negative blood test even if he obtains one, lest he thereupon shorten his course of treatment. *Treat by schedule and not by serologic test* is the slogan of the best modern practice.

The failure of the blood test to reverse is more a matter of how treatment is given than of how much treatment. A little treatment continuously given is more than twice as effective as when intermittently applied, and more than four times as effective as when irregularly given. However, prolongation and intensification of treatment, using much arsphenamine and much heavy metal but especially much arsphenamine in the first 3 months promotes good results. Much arsphenamine and much heavy metal is four times as effective as little arsphenamine and little heavy metal

in securing a negative Wassermann within this period when the drugs are continuously used. The good end-results obtained by prolonging continuous treatment for more than a year are more than double those obtained by the same kind of treatment carried through less than a year (49.7 percent versus 24.4 percent).

The Dangers of Little Arsphenamine and the Short Arsphenamine Course

The distressing frequency of the practice, for which physician or patient may be to blame, of giving four or five arsphenamine injections, testing the blood, finding the patient seronegative in an early case, and virtually dismissing him with a few pills, inunctions, or heavy metal injections should be fought with every resource which current knowledge can bring to bear. Consider first infectious relapse. Two-thirds (64 percent) of those patients who received only one to four injections of an arsphenamine with heavy metal relapsed, while of those who received five to nine injections with heavy metal, only one-seventh (14 percent) relapsed. The critical point, then, for a large proportion of patients with early syphilis with respect to the control of their infectiousness, lies between the fifth and the ninth arsphenamine injection. Figures already cited show that 20 injections of an arsphenamine is the approximate number a patient with early syphilis should have in order to avoid becoming a menace to family and community through infectious relapse.

In the nervous system, formerly thought to be injured by an arsenical, it appears that three times as much relapse (neurorecurrence) and other involvement develops if little arsphenamine is administered than if much arsphenamine is used. Here the measure "little" arsphenamine indicates less than 20 injections and "much" arsphenamine more than 20 injections.

With reference again to the fixed positive serologic bugbear, the amount of treatment given is of less importance than the manner of its administration, the superiority of continuous treatment over intermittent, intensive, and irregular treatment being shown by previously cited figures.

The Choice of Drugs

The practicing physician feels himself constantly in need of advice as to the relative merits of one or another drug in the treatment of syphilis. It appears from the Cooperative Clinical Group investigation that the original arsphenamine (606), when used alone is superior in rapidity of action on the blood serologic test, but the deficiencies of neoarsphenamine are to some extent compensated for by its use with a heavy metal and by its employment in a continuous rather than an intermittent system of treatment. Neoarsphenamine is inferior to arsphenamine in that it produces a larger residue

of absolutely irreversible blood serologic tests than does the older drug. Neoarsphenamine, however, although slightly inferior to arsphenamine, is not an inefficient drug, and its greater adaptability and easier application make it, in suitable combination, the preferred drug for the physician engaged in general practice upon whom the ultimate suppression of syphilis is dependant.

It should be noted, moreover, that in irregular treatment there is little choice between the two drugs. In the matter of reactions the two drugs parallel each other and given in terms of reactions per thousand injections, for arsphenamine (606) they show 14.7 for mild and 2.2 for severe reactions; for neoarsphenamine they show 13.7 for mild and 2.4 for severe reactions. These figures are based on 105,942 injections of arsphenamine and 30,779 injections of neoarsphenamine.

In early syphilis, both as to relapse and as to the general effect of treatment, the evidence tends to indicate that the combinations of arsphenamine-bismuth are more effective than those of arsphenamine-mercury. Arsphenamine-mercury combinations may act more rapidly than arsphenamine-bismuth combinations in the first 3 months in reversing the blood serologic test, but the good effect of the arsphenamine-bismuth combinations appears later (that is in the 4- to 12-month reversal group). Particularly in controlling infectious relapse, it appears that in arsphenamine-bismuth combinations relapses occurred in only 3.6 percent, as contrasted with 9.6 percent with arsphenamine-mercury combinations.

Optimum Treatment

Is it possible to define an average amount of treatment that leads to good results? It appears that after 2 years of observation or treatment the largest number of patients obtaining satisfactory results falls in the category of those receiving from 20 to 29 injections of an arsphenamine and a similar amount of heavy metal. Thus 30 injections of the arsenical becomes a therapeutic objective, in place of the "40 or over" suggested by the results of earlier investigators. That heavy metal is a necessary participant in the securing of good results is indicated by the fact that progression and relapse occurred when much arsphenamine and little heavy metal was given in 25.9 percent as compared with 16.5 percent of the patients who received much arsphenamine and much heavy metal (over 20 injections or 120 inunctions).

A System of Treatment Incorporating the Foregoing Principles

From the data thus far presented it appears, then, that the modern system of treatment of early syphilis must be *continuous;* it must employ an arsphenamine and bismuth, the latter intramuscularly; it must call for not

less than 20, and unless special resistiveness is encountered, hardly more than 30 injections of the arsphenamines; and in accordance with the principles generally recognized in the treatment of the disease, the system should call for continued treatment for 1 year after all symptoms and signs of the disease have disappeared. In order to determine this end point blood tests should be taken at least at the beginning of and end of each arsphenamine course and the patient should be warned of the lack of significance of the negative report from the standpoint of the schedule. Weak positives, after a negative has appeared, should be taken as seriously as strong or fully relapsing positives. A spinal fluid examination with quantitatively titered Wassermann, cell count, protein estimation, and colloidal gold test should be made before the end of the arsphenamine phase of treatment or the introduction of any rest period (none to be allowed until after the first year). It is understood that such a system can be carried through only with adequate tolerance on the part of the patient and this tolerance should be conserved in every possible way. If it fails the case becomes one for consultation. The same system should be employed whether treatment is begun in the seronegative or seropositive primary, or in the secondary stage.

An Alternating Continuous Arsphenamine (606)-Bismuth System

The arsphenamine-bismuth alternating system here described is essentially that used in recent years by the clinics of the Cooperative Clinical Group and published in 1929 for the guidance of practitioners (fig. 2).

Figure 2.—*A Scheme of Treatment for Early Syphilis*

Day or week	Arspbenamine	Interim treatment	Blood Wassermann reaction	Remarks
Day				
1	0.3–0.6	----------	1	Arsphenamine dosage for first 3 injections at level of 0.1 gram for eacb 25 pounds of body weigbt. Average subsequent dosage, 0.4 gram, men; 0.3 gram, women. In average patient all lesions heal rapidly and blood serologic test becomes negative during first course. If arspbenamine cannot be used, substitute 10 to 12 doses 0.45 to 0.6 gram neoarspbenamine, or 10 to 12 doses 0.04 to 0.06 gram mapbarsen, the latter preferably every 4 to 5 days. This applies also to subsequent courses.
5	0.3–0.6			
10	0.3–0.6			
Week				
3	.4			
4	.4			
5	.4			
6	.4			
7	.4			
8	----------	Bismuth, 4 doses 0.2 gram and K. I. or Ung. Hg. and K. I.	---------	
9	----------			
10	----------	----------	1	If mercury is used, note overlap of 1 week at end of first and start of second arsphenamine courses. At tbis point a few days without treatment may be dangerous (neurorecurrence).
11	----------			

FIGURE 2.—*A Scheme of Treatment for Early Syphilis*—Continued

Day or week	Arspbenamine	Interim treatment	Blood Wassermann reaction	Remarks
Week				
12	.4	----------	1	Arspbenamine starts, bismutb stops. Watcb for provocative Wassermann reaction after first dose of arspbenamine.
13	.4			
14	.4	----------	----------	Try to prevent lapses in treatment, especially at tbis early stage.
15	.4			
16	.4			
17	.4	----------	1	
18–23	----------	Bismutb, 6 doses or Ung. Hg. and K. I.	----------	Bismutb is better tban mercury. Use it if possible. Examine cerebrospinal fluid, at about tbis time.
24	.4			
25	.4			
26	.4			
27	.4			
28	.4			
29	.4			
30–37	----------	Bismuth, 8 doses or Hg. and K. I.	----------	
38	.4	----------	1	
39	.4			
40	.4			
41	.4			
42	.4			
43	.4	----------	1	Patients with seronegative primary syphilis may cease treatment here, if blood serologic test has always been negative.
44–53	----------	Bismutb, 10 doses or Ung. Hg. and K. I.	----------	Note tbat bismutb or mercury courses are now gradually getting longer—4, 6, 8, and now 10 weeks.
54	.4	----------	1	
55	.4	----------	----------	The average seropositive primary or early secondary patient sbould have at least 5 courses of arspbenamine.
56	.4			
57	.4			
58	.4			
59	.4	----------	1	
60–69	----------	Bismuth, 10 doses or Ung. Hg. and K. I.	----------	It is safer to finisb treatment witb bismutb or mercury ratber than witb arspbenamine.
70–122	Probation.	No treatment----------	6–12	Blood serologic test every montb if possible; at least every otber month.
123	Complete physical and neurologic examination, spinal puncture, and, if possible, fluoroscopic examination of cardiovascular stripe. Tbereafter, yearly pbysical examinations, blood serologic test every 6 to 12 months. If tbe 2 spinal fluid examinations above are negative, this need not be repeated later.			

In general, if neoarsphenamine is substituted for arsphenamine, a longer arsenical course and somewhat shortened intervals, with a dosage scale of 0.45 to 0.75 gram maximum for women, and 0.6 to 0.9 gram for men is advised.

As an optional scheme more in harmony with the trend toward longer courses, 3 series of 10 to 12 injections each of the arsenical drugs may be given. To secure an overlapping of the heavy metal and the arsenical,

believed by some observers to protect against neurorecurrences, begin the bismuth 2, 3, or even 4 injections before the end of the longer arsenical course, continue it through the period in which the arsenical is suspended, and on into the beginning of the next arsenical course. The bismuth is then suspended while the arsenical course is completed.

Physician-Patient Relationship and Responsibility

The physician has it largely in his power to make or mar the outcome for a patient with early syphilis. He is responsible (1) for an adequate technic; (2) for close surveillance as to infectiousness; (3) for reporting to health authorities if his State law requires; (4) for the return of recalcitrants in the infectious stage to treatment; (5) for adequate instruction of his patient as to course, prevention of complications, and transmission of the disease; (6) for instruction as to marriage and procreation. It is, moreover, essential that he establish a rapport with his patient that will hold him to treatment for the time required. In doing this, the following guide to the substance of the first interview or two is helpful. Lay before the patient the facts under these heads:

1. That he has syphilis and present the evidence for the statement.
2. His outlook for "cure" with emphasis on the excellent reward of persistence in early cases.
3. The general facts of infectiousness as previously outlined.
4. The possibility of marriage under medical control with personal cooperation, and the possibility of healthy offspring under prenatal direction and treatment.
5. The necessity for postponement or avoidance of marriage, intercourse, and pregnancy until the infection is under therapeutic control with the arsphenamines.
6. The relative inefficiency of the blood serologic tests as a measure of infectiousness, fitness for marriage, or conception, and "cure."
7. The dangers (relapse, neurorecurrence, serologic irreversibility and treatment-fastness, precocious tertiarism, and malignant syphilis) of inadequate, short-course, and irregular treatment.
8. The lulling into false security produced by the quick disappearance of symptoms under treatment.
9. The probable treatment requirements, including at least a 15-month estimate for early syphilis, whether seropositive or seronegative primary, or secondary.
10. Personal hygiene, control of treatment reactions, and symptoms of infectious recurrence.
11. The need for observation throughout life.
12. Special arrangements (examination of contacts and infection source,

and of family; communication of facts to others; treatment arrangements for travelers and nonresidents).

13. The probable costs and their settlement or adjustment.

CRITERIA OF "CURE" OF SYPHILIS

THE only definite evidence of "cure" of syphilis in man is reinfection. Tissue transfer, the best criterion in the experimental animal, has not yet been shown to be applicable to man. Necropsy evidence is of no practical value in attempting to decide the question of "cure" in a living patient.

Prolonged clinical observation is the only satisfactory standard of "cure." In concrete terms this means, immediately following the completion of treatment, a full year of probation during which the patient receives no treatment, develops no lesions of syphilis, and the blood serologic reaction tested at frequent intervals (at least every 2 months) remains permanently negative. At the end of the year a complete physical and neurologic examination must show no evidence of progress in the disease, especially in the nervous system or cardiovascular apparatus. Furthermore, the absence of involvement of the nervous system must be demonstrated, not only by freedom from neurologic signs but also by a negative examination of the cerebrospinal fluid. A physician who dismisses a patient as "cured" without a routine spinal puncture is criminally negligent.

If a patient completes the requisite amount of treatment and fulfills these fairly rigid criteria during the period of probation, he may be regarded as probably "cured," and, if he desires, allowed to marry. He should not, however, be discharged from further observation. Every effort should be made to keep him under observation throughout life. This is the only assurance which can as yet be offered against insidious unrecognized progression and relapse. After the first probationary year a yearly physical examination and blood test, without repetition of the spinal fluid if previously twice negative, is in order. Teleroentgenographic and cardiologic study of the heart and the great vessels is desirable by the fifth year and thereafter as the physical examination indicates, but at least with repetition in the tenth year. Only by such supervision can the greatest security be insured for the patient.

THE QUESTION OF ROUTINE LUMBAR PUNCTURE

THE value of this procedure is no longer debatable. Lumbar puncture is best carried out in the hospital or the patient's home, chiefly for the sake of avoidance of postpuncture headache, but if this cannot be arranged, it may safely be performed on ambulatory patients (assuming of course that the presence of brain tumor, the only positive contraindication, is excluded). In this case an occasional puncture headache cannot be avoided, but if

there has been no break in technic, the headache is the worst to be expected. Its incidence may be decreased and its severity minimized by using needles of very small caliber, and by insisting that the patient go home to bed for 48 hours. A puncture headache is disagreeable, but it is far outweighed in importance by the information gained from study of the spinal fluid. Spinal puncture should not be attempted by a physician without experience in its technic.

In early syphilis, routine study of the spinal fluid should not be done immediately, but should be deferred preferably until the completion of the second arsphenamine course (about 5 or 6 months after starting treatment). If spinal puncture is performed earlier than this, some abnormal fluids will be overlooked, because insufficient time has elapsed for the appearance of changes in the fluid. Also, if carried out much later certain minor abnormalities will have been cleared up by treatment. If abnormalities are present, the inexperienced physician should seek expert advice as to the best method of modifying treatment. No attempt can be made in this article to discuss special problems of this nature. In late syphilis, the spinal fluid should always be tested before starting treatment.

If the first spinal fluid examination is negative, spinal puncture should nevertheless be repeated as a matter of precaution at the end of the first year of probation. If it is negative at this time, it need not be done again in future years, and the patient may be assured with reasonable certainty that he will never develop clinical neurosyphilis.

The Management of Spinal-Puncture Headache

Puncture headache may be prevented in practically every patient by performing the puncture with the patient in the recumbent position in bed, and by keeping him flat in bed in a horizontal position for 48 hours afterward. This necessitates the use of a bedpan and of someone to assist the patient at mealtimes. He should be warned against sitting up.

If the puncture is done in the office or clinic the patient should be sent home to bed at once, with instructions to remain there, as above advised, for 48 hours. Under these conditions a few patients will develop headaches even when a needle of very small caliber is used. Puncture headache is characterized by its great severity while the patient is in the erect posture, and by its prompt and usually complete disappearance as soon as he lies down. It is sometimes, though infrequently, associated with nausea and vomiting. If a headache occurs, the patient should be reassured, sent to bed for an additional 3 or 4 days, and instructed to drink a great deal of water. The headache is difficult to control with drugs if the patient insists on being up. It commonly lasts 3 or 4 days, but may persist for 2 weeks. It is not serious.

LATENT SYPHILIS

The first essential in the management of a patient with latent syphilis is for the physician to assure himself that the disease is actually latent, i. e., that it is producing no symptoms or physical signs, and that the only evidence of infection is a positive serologic test of the blood. This implies painstaking and complete physical examination with special reference to cardiovascular and central nervous systems, and a negative routine examination of the cerebrospinal fluid. In patients infected more than 10 years, routine teleroentgenographic and fluoroscopic examination of the cardiovascular stripe is also desirable to rule out clinically unrecognizable aortic dilatation. If lesions of late syphilis can be discovered by these means, the disease is not latent and should not be treated as such.

A Standard Plan of Procedure for Early Latent Syphilis

The studies of the Cooperative Clinical Group have shown that early latent syphilis, i. e., within the first 4 years after infection, should be treated exactly in the same manner as early syphilis, using the same drugs and dosage and the continuous method (see p. 52).

The Treatment of Late Latent Syphilis

This group of patients includes those who have had the infection more than 4 years. Here the aim of treatment is to increase the probability of "cure" or "arrest" and to decrease the probability of clinical progression or relapse over the probable result if no treatment is given. In addition, treatment aims at the control of the potential infectiousness of the latent syphilitic.

In late latent syphilis (in contrast with primary, secondary, and early latent syphilis), the continuous method of treatment is desirable but not absolutely essential. Rest periods probably do no harm. Maximum results are obtained with about 20 injections of an arsphenamine (neoarsphenamine may be freely used to replace arsphenamine) combined with large amounts of heavy metal, the latter prolonged over a long period of time.

The natural tendency of true latent syphilis is toward spontaneous "cure" but this tendency is markedly enhanced by treatment. In treated patients followed for 10 or more years, "cure" or "arrest" is accomplished in about 85 percent, as contrasted with 35 percent if no treatment is given, and the probability of clinical progression or relapse is reduced from 20 to 30 percent to 2 to 5 percent.

An outline of treatment which has proved satisfactory in latent syphilis is shown in figure 3.

FIGURE 3.—*Suggested Outline of Treatment for Late Latent Syphilis*

1. Complete and thorough physical examination.
2. Routine test of spinal fluid before starting treatment, or as soon thereafter as possible.
3. Weeks 1–7 Neoarsphenamine, 8 weekly doses, 0.45–0.6 g.
   8–17 Bismuth, 8–10 weekly doses.
   18–25 Neoarsphenamine, 8 weekly doses.
   26–37 Bismuth, 12 weekly doses.
   38–45 Neoarsphenamine, 8 weekly doses.
   46–57 Bismuth, 12 weekly doses.
   58–69 Rest period.
   70–81 Bismuth, 12 weekly doses.
   82–93 Rest period.
   94–105 Bismuth, 12 weekly doses.

At the completion of this amount of treatment, the physical examination should be repeated (though the spinal fluid, if originally negative, need not be retested). Assuming physical evidence of syphilis to be absent at original and recheck examinations, and the spinal fluid to be normal, treatment may be stopped at this point regardless of whether the blood serologic test is positive or negative.

With latent as with early syphilis, treatment should be followed by a lifetime of periodic observation.

THE TREATMENT OF THE PREGNANT SYPHILITIC WOMAN

COOPERATIVE CLINICAL GROUP and other studies have shown that untreated syphilitic mothers will bear only 16 percent of normal nonsyphilitic children, the remaining 84 percent being represented by miscarriages, stillbirths, and living syphilitic babies. These tragedies may be prevented with almost absolute certainty if syphilis in the mother is recognized (routine serologic test of all pregnant women essential!) and treatment begun before the fifth month of pregnancy, and the chance of a syphilitic infant may be markedly reduced if treatment is begun even as late as the ninth month.

The aim of treatment in pregnant syphilitic women is the prevention or "cure" of syphilis in the infant, not in the mother. Regardless of the type of syphilis in the mother, therefore, treatment should be exactly of the sterilizing variety essential in early syphilis, i. e., the continuous method, and the use of an arsphenamine and bismuth in the dosage advised for

early syphilis (see p. 52). These drugs may be given in alternating courses if time permits (treatment started at the fifth month of pregnancy or earlier) or simultaneously if treatment is not begun until the seventh month or later. Uncomplicated pregnancy is not a contraindication to vigorous treatment.

The syphilitic mother should be given early and adequate treatment throughout every pregnancy, whether her own serologic test is positive or negative. It must be remembered, however, that treatment during pregnancy alone, even if it protects the infant, is not enough for the mother. After delivery her treatment should be resumed in the manner appropriate to her type of syphilitic infection.

THE MANAGEMENT OF LATE SYPHILIS

In a publication of this nature, no attempt can be made to provide a detailed discussion of the treatment of late syphilis, especially such complicated forms as hepatic, cardiovascular, and neurosyphilis. Reference should be had to standard texts for this purpose.

In general, treatment is to be guided by the fact that radical "cure" can no longer be accomplished as in early syphilis, and that the best to be hoped for is the alleviation of symptoms, the healing of lesions, the restoration and maintenance of health, and the prevention of further progression or relapse. The "arrest" of the process can usually be brought about by systematic treatment of a conservative character.

In general, also, the best results in the treatment of late syphilis are attained through expert consultative advice; syphilologist and practitioner working together can improve the patient's chance of recovery without materially increasing its cost.

SERORESISTANT SYPHILIS (WASSERMANN-FASTNESS)

The question most frequently asked of the consultant syphilologist is what to do for the patient with a persistently positive serologic test of the blood. Seroresistance depends upon a variety of factors, some of which are now definitely known. These are:

1. The sensitivity of the serologic test employed. With modern tests, small amounts of reagin in the blood are much more readily detected than with older technics; patients in whom serologic reversal was apparently secured in 1925 are likely, if tested in 1938, to be positive now, not because of any change in themselves, but only because the laboratory is better now than it used to be.

2. In early syphilis, seroresistance may be regarded as a manifestation of persistent foci of organisms or progressive activity. In late syphilis, on

the contrary, it may result entirely from the persistence of a well-established immunity.

3. The type of syphilitic infection at the beginning of treatment. The incidence of seroresistance varies from about 10 percent in patients with early syphilis to about 75 percent of those who first come under treatment with general paresis.

4. In early syphilis, three other factors are of importance.

(a) The type of treatment given. Of those treated continuously, only 11 percent are seroresistant; of those treated intermittently, 37 percent; and of those treated irregularly and hapazardly, 68 percent.

(b) Seroresistance is associated with a high proportion (about 40 percent) of asymptomatic neurosyphilis.

(c) Relapse occurs nearly five times as often in seroresistant early syphilis as when serologic reversal is secured by treatment.

5. In late syphilis on the contrary, there is no relationship between seroresistance and type of treatment, or incidence of asymptomatic neurosyphilis, and relapse or progression is no more frequent in seroresistant patients than in those whose tests reverse.

The Management of Seroresistant Syphilis

The preceding discussion has merely provided a background of necessary information for an intelligent consideration of the crux of the entire problem, "What is to be done for the patient who manifests seroresistance".

Before answering this question in detail, it is essential to reemphasize the aims of treatment of syphilis, early or late. These are:

1. The healing of lesions and the relief of symptoms.

2. The maintenance of good health, and the prevention of progression or relapse.

3. And least important, serologic reversal.

Obviously, if the first and second aims can be accomplished, success or failure in the third is, or should be, a matter of complete indifference to physician and patient alike. If the patient can be restored to health and kept so for a life time, seroresistance may be regarded as entirely analogous to the persistence of a positive tuberculin test in a patient recovered from tuberculosis, or a positive Widal test in one recovered from typhoid fever. Efforts to abolish the persistently positive tuberculin test or positive Widal test are agreed to be both unnecessary and futile.

It is easy to tell when the first aim of treatment, the healing of lesions and relief of symptoms, is accomplished. In most patients this can be done within a few days or weeks, and is not necessarily accompanied by any change in the serologic test. How can one tell when the second aim, the maintenance of good health and the maximum possible freedom from progression or relapse, has been obtained? Can this be measured by serologic

reversal or serologic fastness? In early syphilis, probably yes; here, serologic control of treatment is desirable, serologic reversal to be sought, and seroresistance to be feared. In late syphilis, certainly no. The patient's ultimate clinical fate cannot be measured in any degree by what happens to his blood test. The only possible criterion for determination of optimum kind, amount, and duration of treatment is the long-term clinical observation of large series of similar patients given varying kinds and amounts for varying periods of time. Such observation indicates, as pointed out above, that the seroresistant patient, adequately treated, does as well as, or even better than, his supposedly more fortunate brother with serologic reversal.

In patients with early syphilis the high correlation between seroresistance and involvement of the neuraxis makes it imperative immediately to examine the cerebrospinal fluid of every seroresistant patient, or to reinvestigate it if the results of a previous examination were normal. If the cerebrospinal fluid is normal, further continuous intensive treatment will result in serologic reversal almost uniformly within a year, and the same treatment system should be continued for a full year after serologic reversal has occurred.

In patients with late latent syphilis the ever-present necessity for examination of the cerebrospinal fluid and repeated, diligent clinical and roentgenologic search for lesions of syphilis, especially in the cardiovascular, skeletal, and central nervous systems, is made even more urgent by the manifestation of serologic resistance. If lesions caused by syphilis are found, the treatment system is, of course, to be planned accordingly, e. g., in cardiovascular or neurosyphilis. If, however, careful study discloses no demonstrable abnormalities, i. e., the patient truly has latent or healed benign late syphilis, no departure from the usual continuous, intensive treatment system is required, and prolongation of treatment beyond the usual point is unnecessary.

The employment of special measures for the treatment of such patients is neither necessary nor desirable. "High pressure" intensification of treatment by the use of unusually large dosage or short interval is not necessary because it subjects the patient to an increased risk of treatment functions without the offset of an improvement in prognosis. "Drug shopping" is inadvisable except in a few instances which require individualized expert judgment. Finally, and particularly to be condemned as unproved, unnecessary and as imposing an unjustified risk upon the patient, are efforts at reducing a positive serologic test for syphilis to negative by nonspecific methods, especially artificially induced fever. The prolongation of the usual continuous treatment system to two full years, with the additional safeguard to the patient of a lifetime of periodic observation, will accomplish the desired result of maintenance of good health in the vast majority (probably 95 percent) of patients with seroresistant late syphilis.

Syphilis IN MOTHER AND CHILD

Harold N. Cole, M.D., *Cleveland, Ohio*

AND

Philip C. Jeans, M.D., *Iowa City, Iowa*

IN COLLABORATION WITH

Joseph Earle Moore, M.D.
Baltimore, Maryland

Paul A. O'Leary, M.D.
Rochester, Minnesota

Thomas Parran, Surgeon General, *Washington, D. C.*

John H. Stokes, M.D., *Philadelphia, Pennsylvania*

AND

R. A. Vonderlehr, Assistant Surgeon General
Washington, D.C.

From the syphilis clinic of Western Reserve University, the pediatric clinic of the University of Iowa, and the syphilis clinics of Johns Hopkins University, the Mayo Clinic, and the University of Pennsylvania, in cooperation with the U. S. Public Health Service.

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Part I

SYPHILIS IN PREGNANT WOMEN

INTRODUCTION

IN SPITE of the widespread recognition of the magnitude of the syphilis control program which is developing, the details in which the problems of congenital syphilis differ from those of the acquired disease have not been sufficiently emphasized.

Approximately 1 million of the potential mothers of this country have syphilis, and studies have shown that in a group of women who had never received antisyphilitic treatment only 17 percent of the known conceptions resulted in living nonsyphilitic children. The remaining 83 percent terminated in miscarriages, stillbirths, or living children with syphilis. Each year these women with syphilis transmit the disease to at least 85,000 fetuses of which approximately 25,000 die before birth and 60,000 are born alive with syphilis. These 60,000 infants probably represent only about 10 percent of the newly acquired infections with syphilis which occur each year, but these are incomparably more serious than cases of newly acquired syphilis in adults. Both immediately and for the future, the outlook for the infant with early congenital syphilis is more ominous than for the adult with early acquired syphilis.

The high incidence of congenital syphilis and the enormous toll which it takes annually in life, eyesight, and hearing alone is under any circumstances extremely distressing, but at the present is particularly so because this ghastly toll is readily preventable. By facilities which are at present in existence, or could be developed readily, the occurrence of new cases of congenital syphilis could be reduced nearly to the vanishing point within a few years. There are well known obstetrical reasons why the pregnant woman should report for prenatal care early in pregnancy. These have been widely publicized, and although at present only about one-fifth of those who become pregnant seek medical care before the fifth month of gestation, increasingly large numbers of pregnant women are consulting physicians in the period shortly after they are aware or suspect that conception has occurred. By seizing upon and encouraging this tendency and

by proper conduct of the physician consulted, congenital syphilis may b made a rare disease.

As will be shown, prevention of congenital syphilis depends upon thre principles:

1. The recognition before the fifth month of pregnancy of infection wit syphilis in the mother which antedated or coincided with the pregnanc (this implies the necessity for prenatal examination, including a serologi test for syphilis, in the first half of pregnancy).

2. The recognition of syphilis acquired during pregnancy (this implie the necessity of repeating the serologic test for syphilis at least once durin pregnancy, preferably at about the seventh month).

3. The proper treatment for syphilis of all expectant mothers found t have a checked positive serologic test for syphilis.

These principles have long been recognized by metropolitan clinics an by a few private practitioners. Congenital syphilis will be wiped out however, only when every physician and midwife applies these principles

MANNER AND TIME OF INFECTION OF FETUS

The manner of infection of the fetus in utero and the time during preg nancy at which infection takes place have been the subject of much specu lation and somewhat less clinical and experimental observation. Out c these have come the accepted fact that paternal transmission of syphili (i. e., infection of the child from the father without the mother bein diseased) does not occur, and the working hypothesis that infection of th fetus rarely if ever occurs before the fifth lunar month of gestation.

The actual infection of the fetus is thought to begin with spirochetemi (frequently transient) of the mother, a phenomenon which may occu at any time in patients with syphilis but which varies in frequency, intensity and duration depending on the stage of the disease, the presence or absenc of previous treatment, and (especially with the older infections) othe poorly understood factors. In general, however, in the absence of treat ment, the more recent the mother's infection with syphilis, the longer, mor intense, and more frequent the bouts of spirochetemia and, therefore, th greater the chance of infection of the fetus.

The organisms reach the fetal circulation from the maternal circulatio by way of the placenta during one or more of these bouts of spirochetemia From the incomplete evidence available, it seems to be possible in som cases for the placenta to present a barrier through which the organisms d not penetrate. There is also some evidence to indicate that the spirochete may reach the fetal circulation from the maternal circulation through th placenta without causing readily detectable lesions in that organ. I general, however, syphilitic lesions are produced on the maternal side o the placenta by localization there of organisms brought by the materna

rculation; the lesions extend to the fetal side of the placenta, invade the tal circulation, and infection of the fetus occurs.

FFECT ON OUTCOME OF AMOUNT OF ANTISYPHILITIC TREATMENT ADMINISTERED TO MOTHER DURING PREGNANCY. (AFTER McKELVEY AND TURNER)

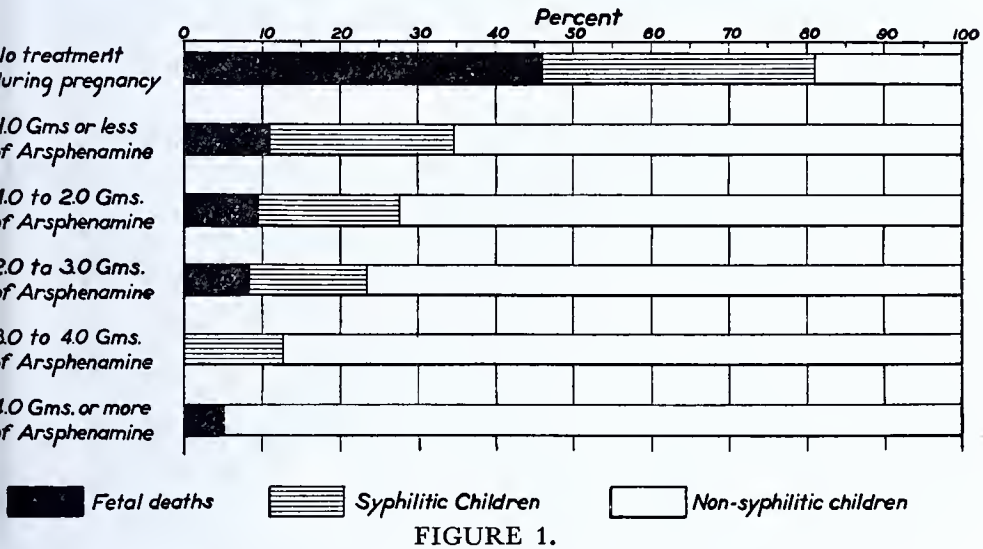

FIGURE 1.

EFFECT ON OUTCOME OF TIME IN PREGNANCY AT WHICH ANTISYPHILITIC TREATMENT IS BEGUN (AFTER McKELVEY AND TURNER)

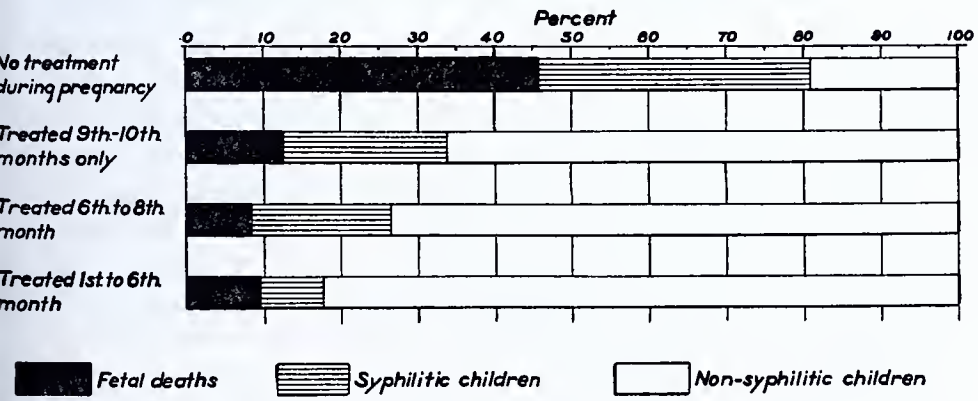

FIGURE 2.

EFFECT OF TREATMENT IN PREVENTING CONGENITAL SYPHILIS

Treatment of the mother for syphilis is an effective way of preventing congenital syphilis in the child. Start treatment early enough, give it intensively enough, and congenital syphilis may be completely prevented. These points are graphically illustrated in figures 1 and 2. In figure 1 it will be seen that there is a direct quantitative relationship between the

amount of antisyphilitic treatment which the mother receives during pregnancy and the percentage of living, nonsyphilitic children. Figure 2 brings out the direct relationship between the duration of pregnancy at the time of onset of antisyphilitic treatment and the incidence of the subsequent birth of normal, nonsyphilitic children.

Obviously the desiderata for the prevention of congenital syphilis are:

1. The recognition of syphilis in every syphilitic pregnant woman before the fifth month of pregnancy, and the immediate institution of antisyphilitic treatment.

2. Intensive and continuous treatment from the time of recognition of syphilis in a pregnant woman until delivery, with emphasis on the arsphenamines because of their spirocheticidal activity.

DIAGNOSIS OF SYPHILIS IN PREGNANT WOMEN

Because of the suppression of clinical manifestations of syphilis in pregnancy, the only practical method for the diagnosis of syphilis in the pregnant woman is by means of routine serologic tests for syphilis. The history which the patient gives is of no help, especially if syphilis and the pregnancy were acquired at or about the same time, and characteristically the physical examination reveals nothing relevant to diagnosing or excluding syphilis. To discover all syphilis complicating pregnancy, therefore, routine serologic tests for syphilis must be done on all pregnant women.

Reliability of Standard Serologic Tests for Syphilis in Pregnancy

Since the diagnosis of syphilis in the pregnant woman must depend almost entirely upon the routine use of serologic tests for syphilis, the question is quite naturally raised as to the effect of pregnancy on the specificity and sensitivity of standard [1] serologic tests.

In spite of statements in the older literature to the contrary, pregnancy does not cause false positive reactions to any of the standard serologic tests for syphilis. In other words, the specificity of these tests is unaltered by pregnancy. The apparent sensitivity of any of the standard tests, however, may be *reduced* by pregnancy because pregnancy may reduce the reagin content of the serum of a woman with syphilis sufficiently to cause a false negative reaction. This is rare, however, with the modern tests of high sensitivity, occurring only occasionally with a patient who has had previous antisyphilitic treatment. Under those circumstances the history or record

[1] Here as elsewhere in this discussion the term "standard serologic test" is used to include all of the serologic tests for syphilis which are in common use and which have shown acceptable specificity and sensitivity in the various serologic conferences conducted under the auspices of the Committee on Evaluation of Serodiagnostic Tests for Syphilis. Those in common use are the Eagle, Hinton, standard Kahn, and diagnostic Kline flocculation tests, and the Eagle and Kolmer complement fixation tests.

previous treatment serves to establish the diagnosis and dictate the proper ourse of action, irrespective of the results of the current test.

Desirability of Test Early in Pregnancy

In figure 2 it is shown that there is a direct relationship between the uration of pregnancy at the onset of antisyphilitic treatment in the yphilitic pregnant woman and the incidence of the birth of normal non-yphilitic children. The earlier treatment is begun the smaller is the ncidence of death in utero from syphilis or the birth of children with the isease. This obviously means, therefore, that it is desirable to establish ne diagnosis at the earliest possible moment. Since it has been shown nat the diagnosis of syphilis in the pregnant woman depends almost entirely pon the demonstration of a positive serologic test for syphilis in the blood, follows that this test must be done as early in pregnancy as possible.

Necessity of Repeating Test Later in Pregnancy

With the serologic tests for syphilis which are at present in routine use, checked negative reaction in a pregnant woman who had not had treat-nent for syphilis in the past gives a high degree of assurance that she did not ave syphilis prior to her pregnancy. This negative reaction, if obtained arly in pregnancy, does not, however, provide a safeguard against two nportant possibilities:

1. That syphilis and the pregnancy might have been acquired at or about ne same time.
2. That syphilis may be acquired after impregnation.

Both of these possibilities are too important to be disregarded. The ormer is obvious, but the latter is too often overlooked. The combination f the two makes it highly desirable to repeat one or more times later in regnancy the serologic test for syphilis upon every pregnant woman who ad a negative reaction to the early first test. For practical purposes, a ngle repeat test may be considered to be sufficient if there is no clinical vidence to raise a suspicion of recently acquired infection with syphilis. o be of greatest use, the repeat test should be done at about the end of the eventh lunar month of gestation. The ideal would be a serologic test at months, again at 5 months, and between the seventh and eighth months.

Obstacles to Routine Tests on All Pregnant Women—A Suggested Solution

Despite the obvious desirability of routine serologic tests for syphilis on ll women early in pregnancy, there are at least two reasons why this esideratum has not been approached:

1. Many pregnant women do not apply for medical care until labor s imminent or actually in progress.

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2. Many practicing physicians have not been convinced of the desirability of routine serologic tests for syphilis upon all pregnant women.

Both of these obstacles may be met by education and by education alone on the one hand of the public, on the other of the physician. As has been pointed out, educational forces are serving to bring more and more pregnant women to the physician or clinic for early routine care. These same forces, however, are powerless in the face of the physician who says "*My* patients do not have syphilis, and I will not insult any one of them by suggesting that she have a serologic test for syphilis performed." The education of such a physician is perhaps impossible. Fortunately, however, the type is in a decreasing minority and today the majority of physicians who practice obstetrics recognize the desirability of the principles which have been outlined even though they have not yet found it possible to apply them to their own practices.

It is regrettable but true that the effectiveness of education both of patient and of physician is at present, to some extent at least, counteracted by practical expediency. The physician who, in his private practice recognizes perfectly well the desirability of detailed prenatal care including routine serologic testing for syphilis, may find that in the circumstances under which he works the amount of effort involved is prohibitive. It is simple enough for the metropolitan hospital clinic which is geared for mass attention to routine to make a serologic test for syphilis a part of the admission examination of every patient. In terms of the human effort involved, however, it is much more difficult for the private practitioner ever remotely to approach the same routine especially if he is carrying a large general practice. The too busy practitioner must somewhere make a compromise; there is no more obvious compromise than to save the effort required to do a routine serologic test for syphilis on every pregnant woman when they are all apparently healthy and come from a social and economic class which leads the doctor to know that he may do a hundred or more routine tests before finding a single positive reaction.

The "effort" factor must not be disregarded. For the man who does so only occasionally, it is a lot of bother to boil a syringe and needle, find a tube and mailing carton and, as requested by some State laboratories, centrifugalize the blood and take off the serum for mailing. The means by which this "effort" factor may be offset are obvious:

1. The actual physical effort involved in doing routine serologic tests for syphilis on all pregnant women should be reduced to a minimum by providing the physician with kits [2] which make the physical business of obtaining blood for a serologic test for syphilis a matter of only a moment's

[2] Many of the State and city and most of the good private laboratories now provide physicians with kits to facilitate the taking and dispatching of blood for serologic testing in a central laboratory.

work provided the physician has reasonable technical skill in performing a venepuncture.

2. Every physician who does obstetrics should adopt as an absolute routine, serologic testing of all pregnant women at the time of the first examination, and at least once later in pregnancy, preferably at about the end of the seventh lunar month of gestation.[3] By so doing the "effort" factor may be eliminated to a great degree; a procedure which is bothersome to an intolerable degree when done occasionally, can be adopted as routine and performed with not a second thought as to the effort involved.

Obviously none of these suggestions even remotely approaches the problem of the prevention of congenital syphilis in children delivered by midwives. In the larger cities there is no effective approach immediately in sight; either midwifery must be outlawed, which seems politically impossible, or the midwives must be educated in the principles of prenatal care, an objective which is practically unobtainable. In smaller communities and the rural districts, however, it has been shown in practice that the supervision of labor by the midwife may be combined readily with proper prenatal care by an established agency. It is to be hoped that a similar arrangement may be developed between the midwives and the large polyclinics in the centers of population in which delivery by a midwife is particularly common.

At the time of writing, 17 States have enacted laws intended to promote routine serologic testing for syphilis in pregnant women. It is too early to pass opinion on the effect of these laws in the prevention of congenital syphilis.

TREATMENT OF SYPHILIS DURING PREGNANCY—AIM

The treatment of syphilis in the pregnant woman is directed entirely toward the fetus; save for a consideration of her ability to tolerate treatment, the status of the infection in the mother is to be temporarily disregarded. It so happens, of course, that in many instances the appropriate treatment system for the welfare of the fetus is also a perfectly satisfactory scheme for the treatment of the mother's infection. If, however, the most desirable methods for treating the mother's infection and protecting the fetus differ (as well they may if, for instance, the mother has general paresis), treatment during pregnancy must be planned for the benefit of the expected child. Proper care of the mother's disease can wait for the few months necessary to secure a full term, healthy infant. The mother's

[3] If the first test is done around 2 months another should be done at the fifth month, and a final one at the seventh or eighth month. If this is not done there is danger of infection in the first few months not being detected and causing irreparable damage before another test is done at 7 months.

welfare must, however, be considered also and signs of intolerance to treatment must not be disregarded.

Considerable confusion exists concerning the exact nature of the effect of antisyphilitic treatment which is given to the mother upon the child in utero. It is obvious that under certain circumstances *prevention* of infection of the fetus must take place. Since both the heavy metals and the arsphenamines readily pass the placental barrier, it is equally apparent that if infection of the fetus has already occurred there is a treatment effect on this infection by drugs administered to the mother. In the actual case, either prevention or cure of the fetal infection may occur, and it may be quite impossible to determine which has occasioned the birth of an apparently normal infant to a woman with syphilis. However, since infection of the fetus rarely, if ever, occurs before the fifth lunar month of gestation, it may be assumed that if antisyphilitic treatment of the mother was begun before this lunar month and was continued with proper intensity and continuity until delivery, the apparently normal child had been prevented from acquiring syphilis and had not been treated for it in utero. The more complicated situations, e. g., the birth of an apparently normal child to a woman with syphilis who was treated only late in pregnancy, will be dealt with in the consideration of the diagnosis of congenital syphilis.

Tolerance of Pregnant Women for Treatment

The general recognition of the fact that pregnancy throws an additional burden on many of the physiologic processes which are also taxed by antisyphilitic treatment has led to some extraordinarily loose thinking and subsequently erroneous conclusions regarding the proper approach to the treatment of syphilis in the pregnant woman. Pregnancy is at best a hazardous undertaking for any woman since she risks her future health and occasionally her life. But having undertaken the basic risks of pregnancy, she stands ready to assume any reasonable additional risk which measurably increases the chance for the birth of a normal child.

In the overwhelming majority of cases the pregnant syphilitic woman tolerates antisyphilitic treatment without difficulty. A rare exception to this tolerance however is the infrequent occurrence of toxic hepatitis and hemorrhagic encephalitis, both of which are very serious reactions and both of which, though extremely rare, occur more frequently in pregnant women than in nonpregnant women or in men.

Since the foregoing considerations have shown the desirability of treatment which is capable of preventing or "curing" the infection in the fetus, it is obviously more desirable to administer the arsenical drugs and the heavy metals in average therapeutic dosage. The additional risk to the mother is small indeed, and so far as available information indicates, is not measurably reduced by the utilization of less than standard

oses of the arsenicals or the heavy metals. Contrariwise it is clear that ıe use of substandard dosage in the treatment of syphilis in the mother *›es* materially increase the chance of the birth of a syphilitic child. For ıe protection of the mother, however, it is essential that while under anti-/philitic treatment she be carefully watched for any evidence of intolerance › arsenic as well as for evidence of beginning damage to the liver and kid-eys, especially considering the strain already placed upon these organs ›y the pregnancy.

Scheme of Treatment

Treatment which is given to the pregnant woman with syphilis seeks ›lely to prevent infection of the unborn child or to "cure" the fetal infec-ion if it has already occurred. The pressing problem is the welfare of he fetus and special forms of treatment desirable for the mother may be ;iven after pregnancy is terminated. For this reason the drugs selected hould be those most effective in combating acute syphilis, i. e., the trivalent ırsenical compounds and bismuth.

Among the numerous arsenical compounds which are proposed for ›yphilotherapy, there are three from which the practitioner should make ıis choice for the treatment of pregnant women with syphilis. There is ıo well documented information to indicate a radical difference in the ›yphilotherapeutic properties of these three drugs in the prevention of ›ongenital syphilis and it is strongly recommended that the physician ıdopt and utilize the one which to him seems the most convenient and lesirable. These compounds are:

1. *Arsphenamine* (606). This is to be given in doses of 0.3 to 0.4 gram at weekly intervals.

2. *Neoarsphenamine* (914). This drug should also be administered weekly in doses of 0.45 to 0.6 gram.

3. *Mapharsen.* This drug should be administered in doses of 0.040 to 0.060 gram, and since it is more rapidly excreted than arsphenamine or neoarsphenamine, it is permissible and perhaps desirable to administer it at intervals of 4 or 5 days.

Bismuth preparation. There is no necessity in the treatment of syphilis in the pregnant woman for employing the more unusual compounds of bismuth. Bismuth subsalicylate suspension in oil is quite satisfactory for all purposes and should be employed in a dose which is equivalent to 0.2 gram of bismuth subsalicylate, or approximately 0.13 gram of metallic bismuth. It must be pointed out that since reliable manufacturers are placing upon the market bismuth subsalicylate suspensions in oil which vary widely in the content of the drug in the vehicle, the physician must be careful to read the label. The proper dose is determined not by the

number of cubic centimeters of the suspension, but by the actual amoun of bismuth subsalicylate which it contains.

Appropriate treatment schemes for syphilis in mothers discovered a various stages in pregnancy are shown in table 1. In this table may be seen three points which must be emphasized:

1. Regardless of the time in pregnancy at which the infection with syphilis of the mother is discovered, her treatment from that point forward should contain a maximum of treatment with an arsenical.

2. Regardless of the duration of pregnancy at the time at which the infection with syphilis in the mother is discovered, treatment should be so planned that she will receive an arsenical in full dose for at least 6 weeks before delivery.

3. In case the infection with syphilis in the mother is discovered late in pregnancy, simultaneous treatment with an arsenical and bismuth should be carried out.

TABLE 1. *Schemes for treatment of syphilis discovered in various stages of pregnancy.*

Week of gestation	Treatment of syphilis discovered in the first trimester of pregnancy	Treatment of syphilis discovered in the second trimester of pregnancy	Week of gestation	Treatment of syphilis discovered in the first trimester of pregnancy	Treatment of syphilis discovered in the second trimester of pregnancy
1	As [1]		21	As	As
2	As		22	As	As
3	As		23	As	As Bi
4	As		24	As	Bi
5	As		25	As Bi	Bi
6	As		26	Bi	Bi
7	As		27	Bi	Bi
8	As		28	Bi	Bi
9	As		29	Bi	Bi
10	As Bi [2]		30	Bi	Bi
11	Bi		31	Bi	As
12	Bi		32	As	As
13	Bi		33	As	As
14	Bi	As	34	As	As
15	Bi	As	35	As	As
16	Bi	As	36	As	As
17	Bi	As	37	As	As
18	As	As	38	As	As
19	As	As	39	As	As
20	As	As	40	As	As

[1] A trivalent arsenical compound—Arsphenamine in 0.3 gram dose. Neoarsphenamine in 0.45 to 0.6 gram dose. Mapharsen in 0.04 to 0.06 gram dose.

[2] Bismuth subsalicylate suspension in oil in 0.2 gram dose.

GENERAL RULES

1. Make minor adjustments in time relationships by adjusting the overlap.
2. Always plan to give an arsenical for at least 6 weeks before delivery.
3. Try to administer at least 20 doses of an arsenical before delivery. If necessary administer mapharsen every 5 days or if very late in pregnancy twice a week.

Management of Pregnant Women Previously Treated

It is well known that we have no clinically applicable criteria for the "cure" of syphilitic infection. It follows, therefore, that every person who has ever had syphilis must be suspected of still harboring some hidden focus of Spirochaeta pallida, even though clinically and serologically he is well and has been well for many years. With regard to the pregnant woman this concept becomes of extreme importance. She may have had syphilis a long time in the past and have been well treated for it; there remains, however, a small but very real chance that she may be capable of transmitting the infection to her unborn child in utero. It becomes obligatory, therefore, to insist that every woman who has or has had syphilis must receive antisyphilitic treatment during every pregnancy, irrespective of the amount of treatment which she has had in the past and irrespective of her apparent clinical status provided she shows no evidence that she is intolerant to the treatment. This is said advisedly and with the full hope that amplification of our information in the future will allow a modification of this particularly severe rule.

Examination of Cerebrospinal Fluid

With the emphasis which is being placed at present upon the necessity of examining the cerebrospinal fluid in all patients with syphilis, there is sometimes the temptation to capitalize the patient's immediate cooperativeness in order to complete the record. It must not be forgotten, however, that since the treatment of the pregnant syphilitic woman is directed entirely towards the fetus and not towards the syphilitic infection of the mother, lumbar puncture during the pregnancy is both unnecessary and for collateral reasons may actually be undesirable. Examination of the cerebrospinal fluid should be deferred to the puerperium or later when it should be performed routinely as in all other patients.

RECAPITULATION

1. Prenatal syphilis is a preventable disease; its prevention depends upon the routine, early, and repeated use of the serologic test for syphilis in every pregnant woman and once the diagnosis is made in the mother, on adequate, early, and continuous treatment of the mother up to the termination of the pregnancy.

2. The pregnant syphilitic woman tolerates antisyphilitic treatment as well as the nonpregnant woman, or man; therefore, for the sake of the expected child, treatment should be as intensive as possible.

3. The treatment of the pregnant syphilitic woman should depend primarily upon the arsenicals because of their spirocheticidal effect, and the effort should be made to administer before delivery at least 20 doses of a trivalent arsenic compound to every pregnant woman with syphilis.

4. Treatment with an arsenical should be supplemented by the intramuscular injection of an insoluble bismuth compound; this should be given between courses of the arsenical if time permits, otherwise concurrently.

5. The welfare of the mother as well as that of the child should be considered and treatment individualized to a sufficient extent to prevent untoward reactions. If the mother shows signs of being unable to tolerate the maximum treatment recommended for the majority of cases it should be reduced until it is well borne.

Part II

CONGENITAL SYPHILIS

INTRODUCTION

FOR PURPOSES of convenience, congenital syphilis is divided into two groups, early and late, depending upon whether the infant is younger or older than 2 years. Early congenital syphilis is in many of its manifestations quite similar to early acquired syphilis. Late congenital syphilis, however, differs in many important particulars from the late acquired disease.

Frank clinical manifestations of early congenital syphilis at birth are nowadays rare. With so many pregnant syphilitic women being recognized and receiving some treatment for syphilis during pregnancy, most of these mothers' children who are born alive are apparently normal at birth. As it is highly desirable to establish the correct diagnosis in the infant born of a mother with syphilis at the earliest possible moment, the prompt diagnosis of early congenital syphilis becomes more and more a problem in laboratory diagnosis.

DIAGNOSIS OF EARLY CONGENITAL SYPHILIS

Since the early diagnosis of congenital syphilis is extremely important from the standpoint of the desirability of immediate treatment in those infants who have syphilis, it is to be regretted that in many instances the correct diagnosis is very difficult to establish in the first few weeks of life. This is because, with one exception which will be pointed out, none of the methods of determining whether or not the child has syphilis is capable of giving an immediate answer. It becomes necessary, therefore, to utilize all of the available sources of information in combination and frequently to make the final decision upon the composite picture.

The ideal methods which should be utilized in attempting to determine whether or not the newborn infant of a woman with syphilis has become infected or not are as follows:

Dark-Field Examination of Scrapings From the Wall of the Umbilical Vein

It is readily apparent that this method cannot be used commonly because of limitations of physical and technical facilities. Where it is possible, however, it is not very laborious to do, and, although a negative result does not exclude the possibility of infection of the child, the finding of Spirochaeta pallida from the scrapings establishes the diagnosis of congenital syphilis in the infant with certainty and at the earliest possible moment.

Quantitative Serologic Tests on the Cord Blood

A routine serologic test on the cord blood is of little value in determining whether or not the infant born of a syphilitic mother has syphilis, since a positive reaction does not necessarily mean that the child has syphilis (it can be produced by reagin [4] which has passed from the maternal circulation through the placenta) and a negative reaction does not guarantee that the child has not sustained infection; he may at the moment be in the seronegative stage. A *quantitative* serologic test on the cord blood, however, serves as a baseline for comparison with similar tests done on the infant's blood at 1, 2, 4, 6, 8, and 12 weeks of life and at periods of 3 months thereafter for at least the first 2 years. In the child who does not have syphilis, tests compared with the positive cord blood reaction will be found to decrease rapidly in titer and to become negative usually before the end of 6 weeks of life; in case the child has become infected the titer may rise steadily with successive tests, or if the infection was sustained very late in intrauterine life, the titer may fall only to rise later. If titration cannot be done, it may be assumed that a positive serologic test of the infant's blood after 6 weeks to 2 months means syphilis. But if the test is negative at 2 months it should be repeated at 6 months, 1 year, and 2 years in a suspected case. If all these tests remain negative the child has certainly escaped syphilis.

Roentgenograms of the Infant's Long Bones at the Age of 2 Weeks

If the mother has received no treatment with bismuth during the pregnancy, an accurate diagnosis of early congenital syphilis may be made on the characteristic roentgenologic pictures of syphilitic osteochondritis at the epiphyseal lines of the long bones, but absence of this finding does not exclude the possibility of syphilis. In mothers who have been treated with bismuth, however, roentgenograms of the bones of many infants who either escaped infection or were cured in intrauterine life exhibit a similar picture

[4] Reagin: The serologist's vernacular for the "positive reaction-producing substance" which is present in the blood serum of patients with syphilis and is not present in the blood serum of normal individuals.

which may be distinguished from syphilitic osteochondritis only with great difficulty.

Clinical Manifestations

If the diagnosis has not been established and treatment instituted sooner, clinical signs of early prenatal syphilis tend to appear within the first 2 or 3 months, if at all. The most common of these are rhinitis (snuffles), skin lesions, and osteitis and periostitis. There is frequently a generalized lymphadenitis, but it has no distinguishing characteristics. If the infection is severe, the baby is puny and ill-nourished, and his appearance frequently has been likened to that of an old man. There may be moderate fever, and, especially in children with snuffles, there may be some degree of nutritional disturbance because of difficulty with nursing. The much emphasized pseudoparalysis is merely voluntary cessation of function due to pain on motion as the result of osteitis and periostitis. Clinical manifestations of neurosyphilis in the infant are more common than is usually recognized; a paraplegia is by no means uncommon.

It must be obvious that the methods for the early diagnosis of congenital syphilis at the moment leave much to be desired. By the time clinical manifestations have developed the serologic test for syphilis will have become positive in most instances. Earlier than this, in "the period of doubt," the diagnosis may be made only upon very careful consideration of the whole picture. As pointed out, demonstration of Spirochaeta pallida in scrapings from the umbilical vein establishes the diagnosis within the first few hours of life; failure to demonstrate the organism, however, does not by any means exclude the possibility that the child has syphilis and under these circumstances a number of weeks may pass before it is possible to judge finally on this most important point. In the meantime, it is essential to keep the infant under close observation with serologic follow-up as described, and roentgenographic studies of the long bones with repeat studies for comparison if they seem desirable.

CLINICAL MANIFESTATIONS OF LATE CONGENITAL SYPHILIS

The clinical manifestations of late congenital syphilis are multitudinous but in general fall into two groups: First, the so-called stigmata which are either scars or developmental anomalies occasioned by active syphilitic processes in the past but which are no longer active; and second, progressive lesions which are active when observed. A mixture of the two may, of course, occur in any one patient.

Some of the important stigmata are listed here.

1. Saddle nose.
2. A curious "dish-shaped" face which is difficult to describe but which is very characteristic in its appearance.

3. Sabre shins (rickets is also a cause).

4. Hutchinson's teeth—barrel shaped, frequently small and notched upper central incisors; also other less characteristic dental anomalies.

5. Frontal and parietal bossing (may be caused by rickets also).

6. Rhagades—radial scars from the mucocutaneous angles of the mouth.

7. Corneal scars, resulting from an old interstitial keratitis.

8. Chorioretinitis, typically peripheral and of the so-called salt-and-pepper variety.

9. Nerve deafness.

The active processes are:

1. Ocular lesions—interstitial keratitis, kerato-iritis, chorioretinitis, primary optic atrophy.

2. Central nervous system disease which may take the form of juvenile paresis but more often resembles the taboparesis of adults. More frequent, however, are the various paralyses (hemiplegia, quadriplegia, or paraplegia) presumably caused by meningovascular syphilis and quite distinct from paresis.

3. Nerve deafness.

4. Lesions of the skeletal system, of which periostitis and osteitis are the most common and symmetrical hydrarthorsis of the knees (so-called Clutton's joints) the most dramatic.

5. Gummatous lesions entirely similar to those seen in adults with acquired syphilis.

Interstitial keratitis is the most frequently found lesion of late congenital syphilis. When it is not treated, the second eye almost invariably becomes involved. Even with treatment, keratitis may develop in the second eye, just as eighth nerve involvement may progress in spite of treatment. Early and persistent treatment in congenital syphilis is a very important factor in the prevention of interstitial keratitis.

In the Cooperative Clinical Group material, 90 percent of the patients with interstitial keratitis had been untreated before the first attack. Only 2 percent of the patients who had been given modern antisyphilitic treatment had interstitial keratitis, as compared with 35 percent of the untreated patients. Extension to the second eye was prevented in 71 percent of the patients who were treated within 6 months of the beginning of this complication. Therefore, the time at which treatment is begun as well as the amount of treatment is important. Treatment is the great factor, however, for six times as many untreated as treated patients lost useful vision.

Treatment of interstitial keratitis with the arsenical compounds and bismuth should be alternating and continuous. If in spite of chemotherapy, relapse or progression of the process or extension to the other eye occurs, nonspecific therapy is indicated. It is also frequently necessary in cases of

evere interstitial keratitis to call in consultation the syphilologist and the phthalmologist.

Late congenital syphilis should be suspected in the presence of any of the linical manifestations listed above and if outspoken may be diagnosed by he expert on clinical grounds alone. In practice, however, the occurrence f any of these clinical manifestations which suggest late congenital syphilis hould prompt the physician to do a serologic test for syphilis; such tests ave a very high degree of reliability in late congenital syphilis.

DISCOVERY OF CONGENITAL SYPHILIS

At any given time only a fraction of the infants and children with congenital syphilis will be suffering so severely from the disease that medical care obviously is necessary. The others are in the stage of latency. Finding these children with latent congenital syphilis and placing them under appropriate treatment before they develop clinical manifestations of late congenital syphilis presents a problem in preventive medicine. Fortunately for the child, it is a simple problem. Syphilis is a disease of the family, and unrecognized congenital syphilis many times may be brought to light by the routine investigation of the entire family of any patient who is found to have syphilis.

The necessity for investigation of the entire family becomes particularly acute when the mother is found to have syphilis, or a child is found to have congenital syphilis. Under all circumstances, however, the discovery of syphilis in any member of the family group should occasion an immediate searching examination of the rest of the family. By this means, the diagnosis of congenital syphilis which has been missed in the neonatal period may be made often before the devastating late lesions of the disease develop.

TREATMENT OF CONGENITAL SYPHILIS

The physician treating congenital syphilis will do well to select a few antisyphilitic remedies and know them well. Instead of attempting to cover the field of arsenic and bismuth preparations, he is wiser to choose two or three potent compounds which are low in toxicity and low in reaction-producing capabilities and administer only these.

Arsenic Preparations

The same arsenic preparations which are recommended for the treatment of the syphilitic mother during pregnancy are also suitable with appropriate adjustment of dosage for the treatment of congenital syphilis in infancy and childhood. In addition, sulfarsphenamine is suitable for *intramuscular use only* in infants in whom the technical problems of weekly vene-

puncture are too great. The appropriate dosages of these drugs [5] are shown in table 2.

TABLE 2.—*Dose (based on body weight) of four arsenicals used in treatment of congenital syphilis*

Drug	Dose	
	Milligrams per kilogram body weight	Grams for 11 pounds (5 kilograms)
Arsephenamine	5–7.5	0.025–0.0375
Mapharsen	0.5–1.0	.0025– .005
Neoarsphenamine	10–15	.050– .075
Sulfarsphenamine	10–15	.050– .075

BISMUTH PREPARATIONS

For routine use the standard preparations of bismuth subsalicylate suspension in oil are quite suitable. The proper dose is 0.002 gram of the compound per kilogram of body weight which amounts to 0.010 gram per 11 pounds of body weight. Here also it must be noted that manufacturers are placing upon the market suspensions with a widely varying concentration of bismuth. *The physician must read the label.*

TECHNIC OF TREATMENT

In general the technic of antisyphilitic treatment in infants and small children is exactly the same as that used in adults with the obviously necessary modifications which are dictated by the difference in the size of the patient. In infants and young children, however, if intravenous treatment is considered necessary, it may be given best into the jugular vein by the following technic: The child is laid on a table with the head dependent and turned to the left or right side. If he does not cry spontaneously during this maneuver it is desirable to make him do so; this brings out the jugular vein very prominently and makes intravenous treatment easy. Under no circumstances should the physician attempt to give an intravenous injection into the fontanel.

[5] In addition to the drugs noted, tryparsamide sometimes is indicated in the treatment of congenital neurosyphilis. The special therapeutic problems therein involved, however, are beyond the scope of this brochure. See Supplement No. 6 to Venereal Disease Information, Management of Syphilis in General Practice.

Reactions to Treatment

In general infants and small children withstand antisyphilitic treatment ell. The reactions which they suffer are identical with or similar to those en in adults and are to be managed by the same methods. The infant ho is ill with early congenital syphilis may, however, do badly under roune antisyphilitic treatment. It is wise, therefore, in instituting the treatent of such patients to practice caution, beginning with heavy metal in nall doses rather than with the arsenicals and seeking at first only to revent further progression, deferring intensive treatment until the general ondition of the infant has been improved.

Table 3.—*Suggested scheme for treatment of congenital syphilis*

Week	Treatment	Week	Treatment
.....	Arsenical in one-third to one-half full dose.[1]	29–40....	Bismuth—note overlap.
		41–48....	Arsenical.
–10.....	Arsenical in full dose.	48–59....	Bismuth—note overlap.
0–19....	Bismuth—note overlap.	60–65....	Arsenical.
0–29....	Arsenical.	65–72....	Bismuth—note overlap.

[1] See text for a discussion of the desirability of instituting treatment even more cautiously in infants ill with active early congenital syphilis.

Suggested Systems of Treatment for Infants and Children

In table 3 will be found a suggested scheme of treatment for infants and children with congenital syphilis. This basic system, which may be employed for children of any age by simply adjusting dosage on the basis of the patient's weight, provides for the administration of 34 doses of an arsenical and 43 of bismuth in 72 weeks.

PROGNOSIS OF CONGENITAL SYPHILIS

The mortality rate of early prenatal syphilis is difficult to estimate with accuracy because it is difficult to assign proper values to death in the immediately prenatal and the immediately neonatal period. Suffice it to say that early active congenital syphilis is a serious disease, but, if the child is born alive and the condition is recognized before a too profound disturbance of nutrition has been occasioned, proper treatment may be effective both in reducing the immediate mortality and in preventing the development of the crippling late manifestations of the disease.

In late congenital syphilis the outlook is more doubtful and relapse and progression occur more frequently. The children rarely die except from juvenile paresis, but they may suffer severe injury from the infection. Untreated interstitial keratitis almost invariably means later involvement of the

second eye, and indeed this may occur even under treatment. Eighth nerve involvement progresses despite treatment. Therapeutic results in symptomatic juvenile neurosyphilis are often disappointing but are usually more than worth the risk involved. Occasionally the results are very good. For the various forms of late congenital syphilis it is especially true that the most satisfactory treatment is prevention. This may be accomplished best by preventing infection of the infant by the proper treatment of the syphilitic mother during pregnancy, but if this fails prevention of late manifestations of the disease by the early recognition and proper treatment of early congenital syphilis.

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Technics of the Eagle, Hinton, Kahn Kline, and Kolmer Tests for the Serodiagnosis of Syphilis

June 1940

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Supplement No. 11

to

Venereal Disease Information

FOREWORD

At the Assembly of Laboratory Directors and Serologists which met in Hot Springs, Ark., in October 1938, the Committee on the Need of Adherence to Conventional Technic in the Performance of Reliable Serologic Tests for Syphilis made the following recommendation:

One of the most important factors responsible for nonadherence to the originator's technic is the failure of many serologists and serologic technologists to keep abreast of new developments. It is imperative that obsolete methods be abandoned. One source of difficulty has been the publication of desirable new modifications in technic by the originators of reliable serologic methods in a number of journals or books, some or all of which are not read by the serologist. To overcome this deficiency, this committee recommends the publication, in complete detail, of the technical procedures to be observed in the performance of each of the reliable, evaluated serologic tests for syphilis now commonly employed in this country. It is recommended that such a publication should be issued by the United States Public Health Service in collaboration with the originators of reliable methods as a supplement to Venereal Disease Information.

It is for the purpose of carrying out this recommendation that the United States Public Health Service is publishing Supplement No. 11 to Venereal Disease Information in which are given the latest modifications of technic as described by the originators of the tests that were demonstrated at the Hot Springs assembly.

Every serologist who originates a test for the diagnosis of syphilis is constantly working to improve his test. The Public Health Service plans to issue revisions of Supplement No. 11 from time to time so that all laboratories may have at hand an authoritative and up-to-date text on the serodiagnosis of syphilis. In the interest of efficiency and accuracy, serologists are urged to adopt the changes advised by the authors of the tests.

EAGLE FLOCCULATION AND WASSERMANN TECHNICS

HARRY EAGLE, M. D.

EAGLE FLOCCULATION TECHNIC (*1*) (*2*) (*4*)

A. QUALITATIVE SERUM TEST

1. *Preparation of serum.*—The clot is centrifuged, and 0.1 cc. of the clear supernatant serum is transferred to a numbered tube. Thick-walled test tubes without lip, measuring 9 to 12 mm. in outside diameter, and 75 to 90 mm. in length, will prove satisfactory. With the larger tubes, it will be found convenient to work with larger quantities, and 0.2 cc. or 0.4 cc. of the serum may be used, with a correspondingly larger amount of antigen.

It is essential that the serum be free of red blood cells or suspended particles which might simulate lipoidal aggregates. The use of strongly hemolyzed serum does not affect the results save insofar as it makes it difficult to recognize aggregates with the naked eye. However, the results can usually be read with no difficulty under the microscope. The serum is inactivated by heating at 56° C. for 20 minutes, or at 60° to 62° C. for 3 minutes (*5*).

2. *Preparation of antigen.*—Fifty grams of dried powdered beef heart (Difco) are extracted for 15 minutes at 30° to 37° C. with 250 cc. of anesthesia ether, with frequent shaking. The mixture is filtered with suction, the ether extract is discarded, and the powder is similarly extracted with a second portion of fresh ether (250 cc.). This is repeated for a total of four extractions. All the ether extracts are discarded. The beef heart powder is then washed on the filter with 100 cc. of fresh ether, thoroughly dried, and extracted with 250 cc. of absolute ethyl alcohol for 3 to 5 days at 20° to 37° C. The flask should be periodically shaken during that interval. At the end of this time the alcohol mixture is filtered, and the moist powder is washed with small portions of fresh absolute alcohol until the combined alcoholic extract and washings measure 250 cc.

All inquiries regarding this test should be addressed to Dr. Harry Eagle, Johns Hopkins Hospital, Baltimore, Md.

This basic extract is fortified with 0.6 percent each of cholesterol and corn germ sterol (6 mg. of each sterol per cc. antigen). The required amount of sterol is added to a measured volume of antigen and is dissolved by boiling.[1] One cubic centimeter of this completed antigen suffices for 500 tests.

Each lot of antigen should be checked by performing several tests with known negative and weakly positive serums. The antigen remains serviceable for years if stored at room temperature in tightly stoppered containers.

3. *Preparation of antigen dilution.*—One volume of the fortified antigen is diluted with 2 volumes of 0.85 percent ("physiologic") NaCl solution. The measured amount of salt solution is blown into the antigen with a pipette. The tip of the pipette should have a sufficiently large bore to make the admixture of salt and antigen rapid and complete. The milky suspension which forms is the stock antigen dilution, which should be aged for at least 24 hours in the ice box before being used. Stored in the ice box, this primary dilution remains serviceable for at least 5 days.

For actual use in the test, a measured amount of this stock dilution (e. g., 0.2 cc.) is further diluted with 8 volumes (e. g., 1.6 cc.) of 4 percent NaCl. This second dilution should be made just before the antigen is added to the serum.

4. *Performance of routine serum test.*—One volume of the freshly diluted antigen (i. e., the stock dilution freshly diluted with 8 volumes of 4 percent NaCl) is added to 2 volumes of inactivated serum. Thus, to 0.1 cc. serum add 0.05 cc. of the antigen suspension; to 0.4 cc. serum add 0.2 cc. of the antigen suspension. The serum-antigen mixture is vigorously shaken for 5 minutes. If a shaking machine is used, it should be adjusted to approximately 180 to-and-fro movements per minute, with a 4-cm. stroke. The tubes are then placed in a 37° C. water bath for 30 minutes.[2] At the end of this time, they are centrifuged at 1,500 to 2,000 r. p. m. for 10 minutes. Prolonged centrifugation at excessive speeds is to be avoided, as it causes partial aggregation of the antigen crystals and false doubtful reactions on microscopic examination.

The results are read at once, by either macroscopic or microscopic observation, or both.

5. *Emergency serum test.*—In case of emergency, as for a blood transfusion, the entire test can be completed within 20 to 25 minutes. The serum is inactivated for 3 minutes at 60°–62° C. (*5*), antigen is added as in the routine test, and the tube is shaken for 5 minutes

[1] The beef heart, sterols, or completed antigen can be obtained from the Digestive Ferments Co., Detroit, Mich.

[2] May be omitted if the tubes have been shaken in a mechanical shaker for 5 minutes.

in a shaking machine at 180 complete to-and-fro movements per minute with a 4-cm. stroke. The incubation is omitted. The tube is then centrifuged for 8 minutes at 1,500 to 2,000 r. p. m., and the results are read as in the routine test, to be now described.

6. *Reading of results.*—In general, aggregates are easier to see under the microscope than with the naked eye. It follows that very weakly positive serums may appear doubtful or even negative when viewed macroscopically, and yet the serum-antigen mixture may show unmistakable aggregation by microscopic examination. Whenever feasible, it is therefore recommended that the tests be read both macroscopically in the tube, and microscopically by pouring a little of the serum-antigen mixture onto a glass slide. If the number of tests makes this prohibitively laborious, it is suggested that the microscopic examination be used wherever there is the slightest doubt as to the macroscopic reading. Almost all otherwise doubtful reactions are thus resolved into positive or negative.

(*a*) *Macroscopic reading.*—In a positive result, a few coarse aggregates are seen floating in a comparatively clear fluid. In a few positive serums, the fluid is water-clear and the aggregates have sedimented to form a coherent flake at the bottom of the tube. If the aggregation is questionable, the result is doubtful. In a negative result, the tube at rest seems opalescent and homogeneous; when it is gently shaken, a swirl of the refractile crystals of the antigen is seen. Occasionally, these discrete crystals are floated to the top of the serum on centrifugation; these immediately redisperse on mild agitation and are readily differentiated from the coherent aggregates of a positive result. Vigorous shaking of the contents of the tube is to be avoided, as sedimented dirt particles or red blood cells are thus resuspended.

(*b*) *Microscopic reading.*—The contents of the tube are poured onto a glass slide. It is convenient to use hollow ground slides, with depressions 1.5 cm. in diameter and 1.5 to 2 mm. deep. If these are not available, circles 2 cm. in diameter are inscribed on ordinary slides with a glass marking pencil. It is essential that not more than 2 minutes elapse between the time the serum-antigen mixture is poured on the slide and its examination under the microscope. The magnification should be about 100-fold (10X ocular, 16 mm. objective). The light should be adjusted so that a control negative serum appears homogeneous (fig. 1F) and should be kept in that position while the actual tests are read.

In a positive result, irregular aggregates of varying degrees of coarseness are seen floating in a clear fluid (figs. 1A to D). If the aggregation is questionable, the result is doubtful (fig. 1E). In a negative result, a uniform distribution of minute and discrete antigen crystals is seen over the entire field (fig. 1F).

7. *Reporting the results.*—In reporting the results to the physician, if the macroscopic reading is positive or doubtful and the microscopic reading is positive, the test is reported as "Positive" (figs. 1A to C).

If the macroscopic reading is negative, but unmistakable aggregates are seen under the microscope, the test is none the less positive (fig. 1D). If there is sufficient serum for a repeat test, such discrepancies should be checked before being reported. If the result has been so confirmed by a repeat test, the report should include a statement to that effect ("Positive—confirmed by duplicate test").

If the microscopic examination shows indefinite aggregation (fig. 1E) the macroscopic reading is almost invariably negative, and the test is reported as "Doubtful. Please repeat." If there is sufficient serum for retesting, such results should be checked before being reported.[3] The report should include a statement to that effect ("Doubtful—confirmed by duplicate test. Please repeat").

B. QUANTITATIVE SERUM FLOCCULATION TEST

If it is necessary or desirable to ascertain the degree of positivity of a known positive serum, this can be done by carrying out the routine test on serial dilutions of serum as shown in table 1.

TABLE 1

Whole inactivated serum, cc	0.2	0.1	0.05						
Serum, diluted 1:8 with 0.85 percent NaCl, cc				0.2	0.1	0.05			
Serum, diluted 1:64 with 0.85 percent NaCl, cc							0.2	0.1	0.05, etc.
0.85 percent, NaCl, cc	0	.1	.15	0	.1	.15	0	.1	.15
Final dilution of serum	1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256
Result of test	+	+	+	+	+	+	±	0	0

The serum is positive up to a 1:48 dilution, a reagin titer of 48.[4]

C. SPINAL FLUID TEST

Although the ice box Wassermann technic is to be preferred for the examination of spinal fluids because of its greater sensitivity, the microflocculation procedure gives satisfactory, even if not optimum, results.

To 1.0 cc. of fresh fluid are added 0.1 cc. of the final antigen dilution, prepared as already described for the serum flocculation test. The mixture is shaken, centrifuged, and read as previously described.

The test can be performed quantitatively by using graded quantities of spinal fluid as indicated in the following table:

Spinal fluid, cc	1.0	0.4	0.2	0.1	0.05
0.85 percent NaCl, cc	0	.6	.8	.9	.95
Antigen suspension, cc	.1	.1	.1	.1	.1

[3] Since 2 hours suffice for the entire test, it can be repeated on the same day if the serum is available.

[4] Very rarely, zone reactions are observed in which strongly positive serums give a negative result in the routine test with whole serum but are strongly positive if tested in a 1:10 or 1:20 dilution.

FIGURE 1A.—Macroscopic reading, positive—a single large clump of antigen floating in clear liquid; microscopic reading, positive; report to physician, positive.

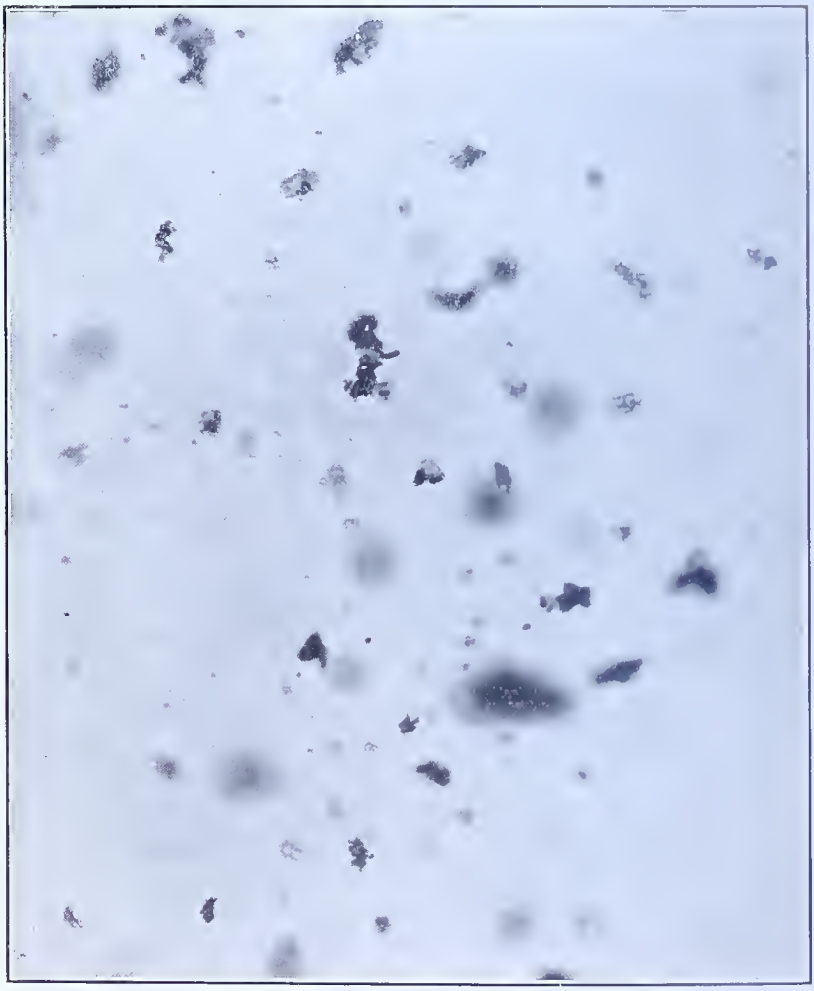
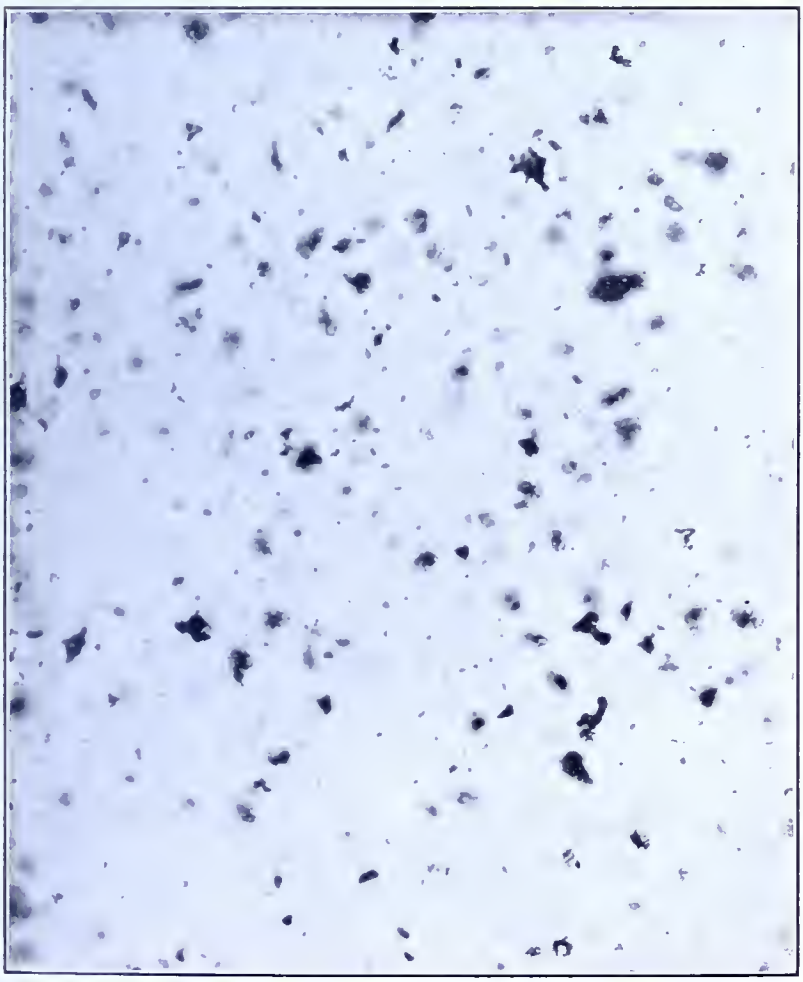


FIGURE 1B.—Macroscopic reading, positive—numerous clumps floating in clear liquid; microscopic addition, positive; report to physician, positive.



C.—Macroscopic reading, doubtful—indefinite small aggregates; microscopic reading, positive; report to physician, positive.

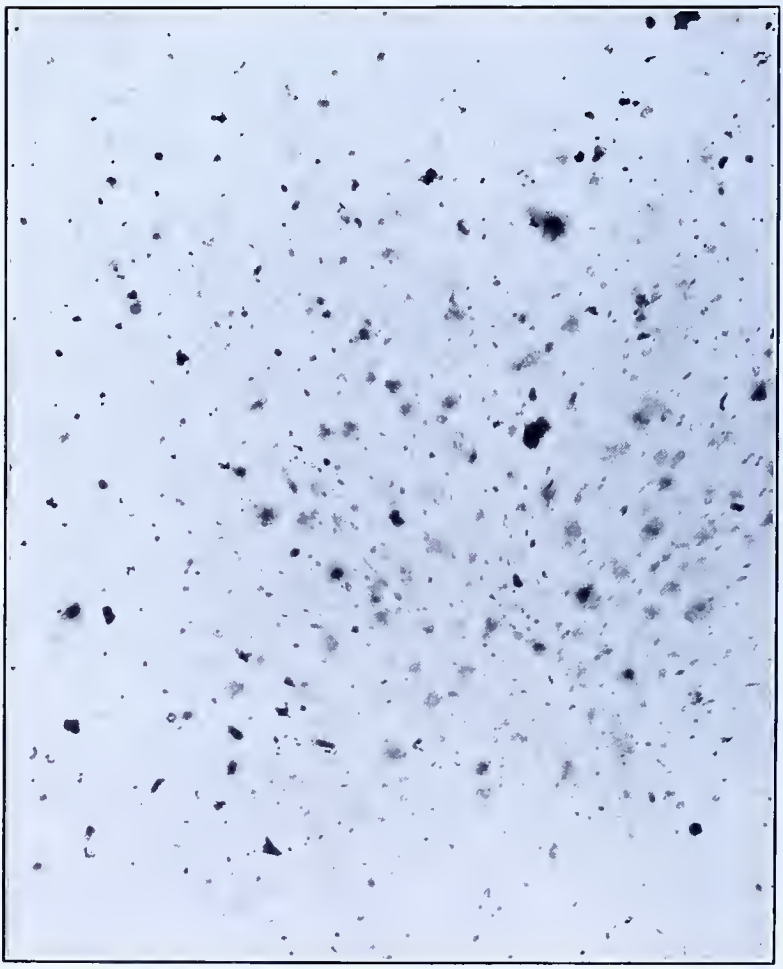


FIGURE 1D.—Macroseopie reading, negative—apparently homogeneous; mieroseopie reading, positive; report to physieian, (1) positive, please repeat, (2) positive, eonfirmed by duplieate test; please repeat.

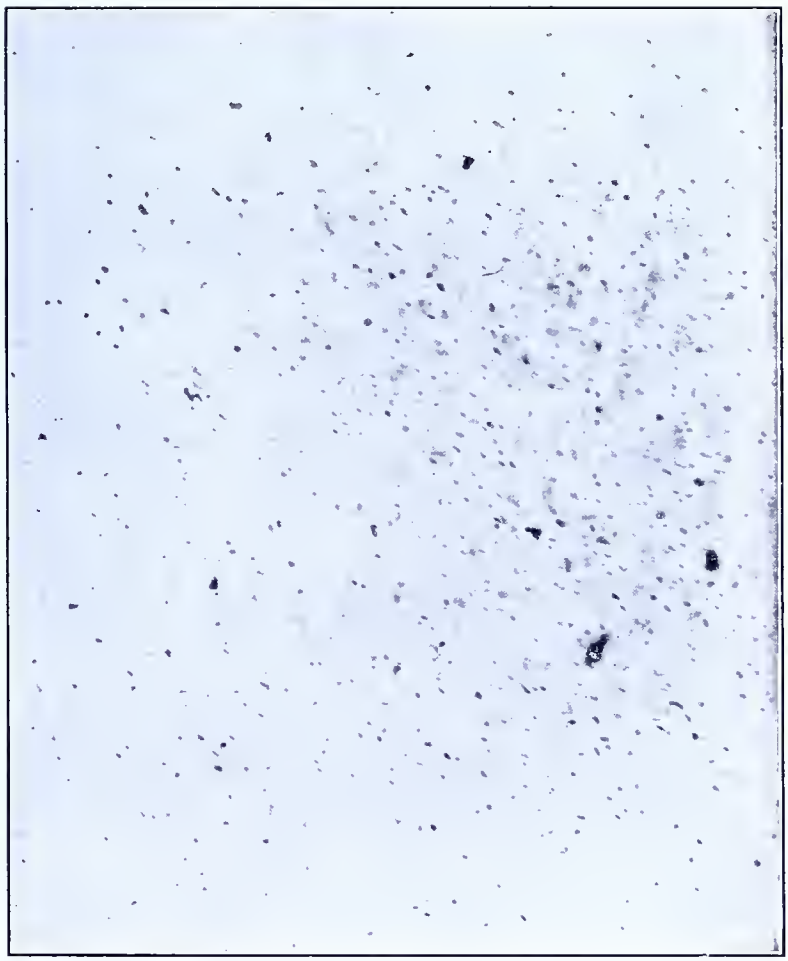


FIGURE 1E.—Macroscopic reading, negative; microscopic reading, doubtful; report to physician, (1) doubtful, please repeat, (2) doubtful, confirmed by duplicate test; please repeat.

FIGURE 1F.—Macroscopic reading, negative; microscopic reading, negative; report to physician, negative.

EAGLE WASSERMANN TEST [5] (*1*) (*3*)

1. *Preparation of antigen.*—If a uniform preparation of dried powdered beef heart is not available, the technician may prepare his own. The heart tissue must be quite fresh, and the fat, pericardium, and the blood vessels should be removed. The muscle is ground in an ordinary meat grinder, and then dried by the addition of 150 cc. of acetone to each 100 grams of tissue. After about an hour at room temperature, with frequent shaking, the acetone is removed by filtration, the tissue is shaken with a second portion of acetone (150 cc.) for a few minutes, and the mixture again filtered. The acetone filtrates are discarded. The tissue is spread in a thin layer on a clean surface and thoroughly dried in a 37° C. incubator for 24 hours, when it is turned and dried again for 24 hours. The dry sheet is now pulverized as finely as possible in a mortar, or preferably, in a pulverizing machine.

(*a*) *Preparation of the tissue extract.*—50 grams of the dried powdered beef heart, preferably a pooled preparation such as those available commercially (e. g., Difco), are extracted with 250 cc. of pure anesthesia ether (5 cc. per gram powder) for 15 minutes at 30° to 37° C., with frequent shaking. The mixture is filtered with suction, and the extraction is repeated with fresh ether for a total of 4 extractions. All the ether extracts are discarded. After the fourth filtration, the beef heart powder is washed on the filter with 100 cc. of fresh ether, dried, and then extracted for 5 days with 250 cc. of absolute alcohol (5 cc. per gram powder). The alcohol extract is filtered, and the moist powder is washed on the filter with small portions of fresh alcohol until the volume of the combined alcoholic filtrate and washings is equal to 250 cc. (5 cc. per gram powder). The clear, straw-yellow extract is the basic antigen, and contains approximately 1.2 to 1.5 percent solids. It is now fortified with cholesterol, which is added to a concentration of 0.6 percent (6 mg. per cc. extract).[6] The cholesterol is dissolved by boiling. This completed antigen, tightly stoppered, retains its reactivity almost indefinitely (more than 8 years) at room temperature. For use in the test, it is diluted fresh each day by slowly pouring from 80 to 200 volumes of 0.85 percent salt solution into 1 volume of the antigen. The exact quantity of salt solution to be used is determined once for each lot

[5] (Inactivated serum; pooled guinea-pig complement; sheep red blood cells; rabbit amboceptor; strongly fortified beef-heart antigen. All the reagents are used in a volume of 0.4 cc. making the total volume of the test 2 cc. If the conservation of materials is advisable or if the technician is sufficiently expert, all the indicated quantities can be halved.)

[6] In a large laboratory, in which the complement is pooled from many pigs and is uniformly of high activity, 1 percent cholesterol may be used with safety with somewhat more sensitive results. With such highly fortified antigen, 3 hours in the ice box followed by one-half hour at 37° C. is the recommended incubation period. Particular care must be paid to the complement and antigen controls.

of antigen by the technic to be described. One cubic centimeter of antigen suffices for approximately 100 tests.

It is to be noted that the same basic extract, fortified with 0.6 percent cholesterol and 0.6 percent corn germ sterol, is used in the Eagle flocculation technic previously described.

(*b*) *Anticomplementary and hemolytic titration of antigen.*—Each lot of antigen should be tested once for its anticomplementary and hemolytic activity, to ensure that these undesirable properties are not so pronounced as to interfere with its use in the test. The technic of these titrations is given in tables 2 and 3. Antigens prepared by the method just described are usually not anticomplementary in more than a 1:6 dilution and are not significantly more hemolytic than pure alcohol. The use of a 1:120 dilution in the test proper (vide infra) thus provides a wide margin of safety.

TABLE 2.—*Hemolytic titration of antigen*

	Antigen dilution*						
	1	1:2	1:3	1:4	1:6	1:8	1:12
Antigen dilution, cc	0.4	0.4	0.4	0.4	0.4	0.4	0.4
0.85 percent salt solution, cc	.8	.8	.8	.8	.8	.8	.8
Cell suspension, cc.†	.8	.8	.8	.8	.8	.8	.8
HEMOLYSIS IS READ AFTER ½ HOUR AT 37° C.							
Example of reading of hemolysis	Complete	None	None	None	None	None	None

Conclusion: The antigen is not significantly hemolytic.

*These dilutions are readily prepared by the following procedure:

Whole antigen, cc	0.4	0.2	0.13	0.1	0.07	0.05	0.035
Salt solution, cc	0	.2	.27	.3	.33	.35	.37
Final dilution of antigen	1	1:2	1:3	1:4	1:6	1:8	1:12

†Can be sensitized or unsensitized, but should be 1.5 percent by volume.

TABLE 3.—*Anticomplementary tritration of antigen*

	Antigen dilution*						
	1	1:2	1:3	1:4	1:6	1:8	1:12
Antigen dilution, cc	0.4	0.4	0.4	0.4	0.4	0.4	0.4
0.85 percent salt solution, cc	.4	.4	.4	.4	.4	.4	.4
Complement, 1:10, cc	.4	.4	.4	.4	.4	.4	.4
AFTER 4 HOURS AT 0° TO 5° C., FOLLOWED BY ½ HOUR AT 37° C., ADD 0.8 CC. OF SENSITIZED CELLS TO ALL THE TUBES							
Example of reading of hemolysis after ½ hour at 37° C.	Complete	0	0	Partial	Complete	Complete	Complete

Conclusion: Antigen is antieomplementary up to 1:4 dilution.

*These dilutions are readily prepared by the following procedure:

Whole antigen, cc	0.4	0.2	0.13	0.1	0.07	0.05	0.035
Salt solution, cc	0	.2	.27	.3	.33	.35	.37
Final dilution of antigen	1	1:2	1:3	1:4	1:6	1:8	1:12

(*c*) *Determination of the optimum antigen dilution.*—As in the case of the anticomplementary titration, the optimum dilution of the antigen need be determined only once with each lot of antigen. The importance of this titration is not generally realized. A typical titration illustrating the method is given in table 4. In this example, the most sensitive, and thus the optimum dilution, is approximately 1:140. If the powdered beef heart used for the antigen is a pooled, uniform product and if the method of preparation is adhered to rigidly, it is generally found that the optimum antigen dilution is also quite uniform not deviating significantly from the 1:120 to 1:160 value of the following titration.

TABLE 4.—*Determination of the optimum antigen dilution*

Antigen dilution *	Strongly positive serum	Result of Wassermann test on the same serum diluted with salt solution						
		1:2	1:4	1:8	1:16	1:32	1:64	1:128
1:40	+	+	+	±	0	0	0	0
1:80	+	+	+	+	±	0	0	0
1:100	+	+	+	+	+	0	0	0
1:120	+	+	+	+	+	±	0	0
1:160	+	+	+	+	+	±	0	0
1:200	+	+	+	+	+	0	0	0

+=positive (no hemolysis).
±=doubtful (partial hemolysis).
0=negative (complete hemolysis).

*The antigen dilutions to be used in the above-mentioned titration can be prepared as follows:

1:40 antigen dilution cc	8.0	4.0	3.2	2.7	2.0	1.6
Salt solution, cc	0	4.0	4.8	5.3	6.0	6.4
Final dilution of antigen	1:40	1:80	1:100	1:120	1:160	1:200

Similarly, the serum dilutions can be readily prepared as follows:

Serum, cc	4.0	2.0	1.0	0.5	0.25	0.125	0.062
Diluent, cc	0	2.0	3.0	3.5	3.75	3.9	4.0
Final dilution of serum		1:2	1:4	1:8	1:16	1:32	1:64

In preparing the antigen for daily use in the test, the correct volume of salt solution is slowly poured into one volume of antigen. The antigen dilution should be opalescent and homogeneous, containing no visible granules.

2. *Preparation of complement.*—At least five, and preferably more, guinea pigs are bled from the heart; the clots are broken up with a glass rod and centrifuged. Bleeding large pigs (more than 1 pound in weight) for comparatively small quantities (5 to 10 cc.) at intervals of 4 to 6 weeks, is more economical than exsanguinating the animal.

The small laboratory which cannot pool the fresh serum of several pigs for each series, or which cannot obtain such pooled fresh serum from a central source of supply, may have recourse to three methods of preservation. (1) Multiple containers of complement serum may be vacuum-dried from the frozen state and vacuum-sealed on the Flosdorf-Mudd apparatus.[7] Such complement remains fully active

[7] The Flosdorf-Mudd apparatus is being manufactured by the F. J. Stokes Co., East Tabor Road, Olney, Philadelphia, Pa.

for at least 10 months if stored in the refrigerator. (2) Although complement retains its activity, when frozen at very low temperature (< 20° C.), over a period of weeks and even months, such freezing is not feasible in the ordinary laboratory. (3) Complement may be preserved by the addition of salt. Numerous methods of "salting" complement have been recommended. As simple and as satisfactory as any is the addition of sodium chloride in bulk to the complement serum (80 mg. of NaCl per cc. serum, dissolved by shaking). For actual use in the test, the salted complement is diluted with 9 volumes of water (e. g., 1 cc. complement+9 cc. distilled water) to make a 1:10 dilution.

Perhaps the most satisfactory method of preserving complement in the small laboratory is a combination of (2) and (3)—the container of salted complement is placed in the freezing compartment of a mechanical refrigerator. So stored, it undergoes no demonstrable deterioration in 2 weeks.

3. *The preparation of the serum or spinal fluid to be tested.*—The coagulated blood is separated from the sides of the tube with a clean glass rod and centrifuged for 5 to 10 minutes at 1,000 to 1,500 r. p. m. 1 cc. of the clear serum is pipetted into a numbered tube, which is then placed in a water bath at 56° C. for 15 to 20 minutes.[8] An incompletely coagulated specimen, or one prevented from coagulating by the addition of oxalate or citrate (neither of which should be used in the Wassermann reaction), will develop a precipitate of coagulated fibrinogen upon inactivation. Contrary to published reports, even large amounts of hemoglobin dissolved in the serum do not per se affect the results save so far as they obscure the reading of hemolysis. Similarly, the only objection to blood older than 24 hours is the fact that it tends to become anticomplementary with age, particularly if conditions facilitate multiplication of bacteria. Whenever feasible, the serum should be inactivated immediately before testing. If it is inactivated the day before the actual test, it should be reheated for 5 minutes at 56° C. before proceeding with the test on the following day.

Native amboceptor for sheep cells may be removed from the inactivated serum by adding 0.1 cc. of a thick (20 to 40 percent) suspension of washed sheep cells to each cubic centimeter of inactivated serum. The serum and cells are thoroughly mixed and centrifuged 5 minutes later in order to remove the cells. An alternative method is to add the thick sheep cell suspension to the whole cold blood, mix throughly with a clean rod, and centrifuge after 15 minutes in the refrigerator. The latter procedure has the advantage of simplicity, for it eliminates

[8] In an emergency, the serum may be inactivated for 3 minutes at 60° to 62° C.

the necessity of a double centrifugation for each serum; it has the disadvantage of causing slight hemolysis.

The removal of native amboceptor unquestionably results in an increased sensitivity. Nevertheless, it is perhaps an unnecessary complication if a flocculation test is carried out in parallel with the Wassermann. The flocculation test ensures the detection of practically all serums which might be Wassermann negative because of their native amboceptor content.

Spinal fluid contains neither complement nor amboceptor in significant quantities, and therefore requires neither inactivation nor the absorption of native amboceptor. The whole fresh fluid is used as such.

4. *Salt solution.*—The salt solution used in diluting antigen, complement, serum, cells, and amboceptor is a 0.85 percent solution of C. P. NaCl in distilled water. It is advisable but not absolutely necessary to add a trace of alkaline buffer, as old distilled water may be sufficiently acid because of dissolved CO_2 to accelerate the deterioration of dilute complement. It is convenient to keep a stock solution of 17 percent NaCl. Fifty cc. of this is diluted with 950 cc. of distilled water to form the 0.85 percent solution used in the test.

5. *Setting up the tests.*—(*a*) *Routine qualitative serum tests.*—Three tubes are advisable, although only two are essential. Tube 1 is the serum control, containing serum and complement, but salt solution instead of antigen.

	Serum control	Test proper	
Whole serum, cc	0.2	0.2	0.1
Complement, 1:10, cc	.4	.4	.4
Antigen dilution, cc	0	.4	.4
0.85 percent NaCl, cc	.6	*.2	*.3

*May be omitted.

Tubes 2 and 3 are the test proper, each containing 0.4 cc. complement, 0.4 antigen, and different quantities of serum (0.2 and 0.1 cc.). The addition of salt solution to tubes 2 and 3 is not essential, but serves to bring the total volume in all three tubes up to 1.2 cc., corresponding to 0.4 cc. of each of the three reagents.

One antigen control suffices for the entire series of tests, and two complement controls are also set up, as here indicated.

	Antigen control	Complement controls (in duplicate)				
Antigen dilution, cc	0.4	0.4	0.4	0.4	0.4	0.4
Complement, 1:10, cc	.4	.4	.2	.13	.1	0
Salt solution, cc	.4	.4	.6	.7	.7	.8

(*b*) *Quantitative serum tests.*—If a quantitative determination of the reagin content of a known positive serum is desired, a series of serum dilutions may be prepared by placing 0.4 cc. of salt solution in each of a series of tubes. To the first tube is added 0.4 cc. of serum, and 0.4 cc. of the resulting mixture is transferred to the following tube; 0.4 cc. is withdrawn from tube 2 and transferred to tube 3, and the process is repeated with all the tubes of the series. The final set-up is then as follows:

Serum control	Test proper							
Serum, cc., 0.2	0.2	0.1	0.05	0.025	0.0125	0.0062	0.031	
	in a total volume of 0.4 cc. corresponding to a dilution of							
	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256

It is a technically simpler procedure to prepare a single 1:20 dilution of the serum (0.1 cc.+1.9 cc. salt solution) and distribute the serum as follows:

Whole serum, cc	0.2	0.05				
Serum, 1:20, cc			0.4	0.2	0.1	0.05
Salt solution, cc	.2	.35	0	.2	.3	.35

The dilutions so obtained are 1:2, 1:8, 1:20, 1:40, 1:80, 1:160, in a volume of 0.4 cc. This is the recommended procedure. Antigen and complement are then added exactly as in the routine test (0.4 cc. of each dilution).

(*c*) *Spinal fluid Wassermann test.*—The routine spinal fluid Wassermann is a quantitative test. Except for the quantities used and the fact that the fluid is not inactivated, the set-up of the test is similar to that of the quantitative serum test:

	Spinal fluid control	Test proper						
Spinal fluid, cc	1.0	1.0	0.6	0.4	0.2	0.1	0.05	0.025
Complement, 1:10, cc	*.2	*.2	.2	.2	.2	.2	.2	.2
Antigen dilution, cc	0	*.2	.2	.2	.2	.2	.2	.2

*The quantities of the reagents are halved in order to conserve spinal fluid. It is to be noted that the maximum amount of spinal fluid used relative to the other reagents is 10 times that used in the serum tests.

The entire series, serum and spinal fluid tests and controls alike, are then placed in the ice box for 3 to 4 hours.

While the tests are in the ice box, the sensitized cell suspension is prepared and tested.

6. *Preparation of the sensitized cell suspension.*—Because this technic calls for the use of a fixed quantity of a pooled, standard

complement, it becomes possible to set up the diagnostic tests as the first step in the daily performance of the Wassermann reaction, to place these tests in the refrigerator for their primary incubation of 3 to 4 hours, and then proceed to the preparation of the sensitized cell suspension. The cells can be washed, the amboceptor titrated, and the titration checked within 2 hours. This leaves ample time for other routine work before the tests are placed at 37° C. for their secondary incubation of 30 minutes prior to the addition of the cells.

(*a*) *Preparation of the stock 3 percent suspension of sheep cells.*—Citrated sheep blood (1 part of 5 percent citrate and 5 to 10 parts of blood) or defibrinated blood is collected as aseptically as conditions permit. The method of choice is to bleed the animals from the jugular vein into a sterile vessel containing the citrate. The addition of sucrose in bulk to a concentration of 2.5 percent (2.5 grams per 100 cc. blood) serves to postpone their spontaneous disintegration. Sterile sheep blood generally remains serviceable for 1 to 3 weeks if stored at 0° to 5° C.

For use in the test, 1 volume of blood is washed with 10 to 15 volumes of 0.85 percent salt solution, the mixture is centrifuged, and the supernatant fluid carefully withdrawn. The sedimented cells are resuspended in a second portion of salt solution and again centrifuged, this time in a graduated tube, until the volume of sedimented cells becomes constant. Ten to 15 minutes at 2,000 to 2,500 revolutions per minute suffice. The supernatant fluid is carefully withdrawn, and the measured cell sediment is resuspended in 32 volumes of salt solution to form the stock 3 percent suspension of unsensitized cells. This must be prepared fresh daily.

(*b*) *Titration of amboceptor.*—The minimal hemolytic quantity (unit) of amboceptor must be determined daily for the particular cell suspension to be used that day, by the technic of table 5. This hemolytic unit of amboceptor should be a 1:2,400 dilution or higher; and an amboceptor should be discarded if it is so inactive that the hemolytic unit represents, e. g., a 1:1,000 dilution.

The unit of amboceptor in the example cited is a 1:3,000 to 1:4,000 dilution, or, interpolating, approximately a 1:3,500 dilution. An amboceptor dilution is now prepared containing 2½ units (in the example cited, a 1:1,400 dilution). This amboceptor dilution is poured into an equal volume of the 3 percent cell suspension to form the 1½ percent suspension of sensitized cells which is actually used in the test.

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TABLE 5.—*Technic of amboceptor titration*

	Amboceptor titration *						
	1:1000	1:1500	1:2000	1:3000	1:4000	1:6000	1:8000
Amboceptor dilution, cc	0.4	0.4	0.4	0.4	0.4	0.4	0.4
3 percent cell suspension, cc	.4	.4	.4	.4	.4	.4	.4
Salt solution, cc	.8	.8	.8	.8	.8	.8	.8
Complement, 1:10, cc	.4	.4	.4	.4	.4	.4	.4
Example of reading of hemolysis after ½ hour at 37° C.	Complete	Complete	Complete	Complete	Partial	Partial	None

*The following is a simple method of setting up these amboceptor dilutions:

1:1000 amboceptor, cc	0.4	0.27	0.2	0.13	0.10	0.067	0.05
Salt solution, cc	0.0	0.13	0.2	0.27	0.30	0.34	0.35
Final dilution of amboceptor	1:1000	1:1500	1:2000	1:3000	1:4000	1:6000	1:8000

(*c*) *Check on the amboceptor titration.*—The sensitization of the cells should be completed within an hour. One set of complement controls previously placed in the refrigerator along with the tests, and containing 0.4, 0.2, 0.13, and 0.1 cc. of complement in a total volume of 1.2 cc., is now removed from the refrigerator, and 0.8 cc. of the sensitized cell suspension is added to each tube. The degree of hemolysis is read after 30 minutes at 37° C. If the amboceptor titration was correct, the 0.4 cc. of 1:10 complement used in the test represents 2 to 2½ times the amount necessary to cause complete hemolysis in 30 minutes. Accordingly, the first two tubes of the complement titration should be completely hemolyzed; tube 3 should be partially hemolyzed, and tube 4 should show little or no lysis. Any error in the amboceptor titration becomes immediately apparent. If only the first tube is completely hemolyzed, the cells have been inadequately sensitized, and more amboceptor should be added. If three tubes show complete lysis, an excess of amboceptor has been used. The technician must reconcile himself to a sudden decrease in the sensitivity of the test, or a second portion of blood must be washed and sensitized with the correct amount of amboceptor, somewhat less than that used in the first lot.

7. *Secondary incubation of the tests at 37° C., and the addition of the sensitized cells.*—After 3 to 4 hours at 0° to 5° C., the tests and controls are placed in the 37° C. water bath for 30 minutes. Eight-tenths (0.8) cc. of the sensitized cell suspension is then added to all the tubes, which are vigorously shaken and replaced at 37° for their final incubation of 20 to 30 minutes.

This leeway of 10 minutes is allowed the technician to compensate for any slight error in the sensitization of the cells as detected by the complement check just described. If tube 2 of the complement control, which contains half the amount of complement used in the test, is slow to hemolyze, requiring, for example, 30 minutes for complete lysis, then the tests also are given 30 minutes. If, on the other hand, tube 2 shows complete hemolysis in 20 minutes, the results of

the tests also should be read in 20 minutes after the addition of the sensitized cells. The futility of any stop watch precision is apparent when we remember that it requires 5 to 15 minutes merely to add cells to a large series of tests.

8. *Reading of results.*—(*a*) *The antigen controls* should be completely hemolyzed. Properly diluted, the antigen fortified with 0.6

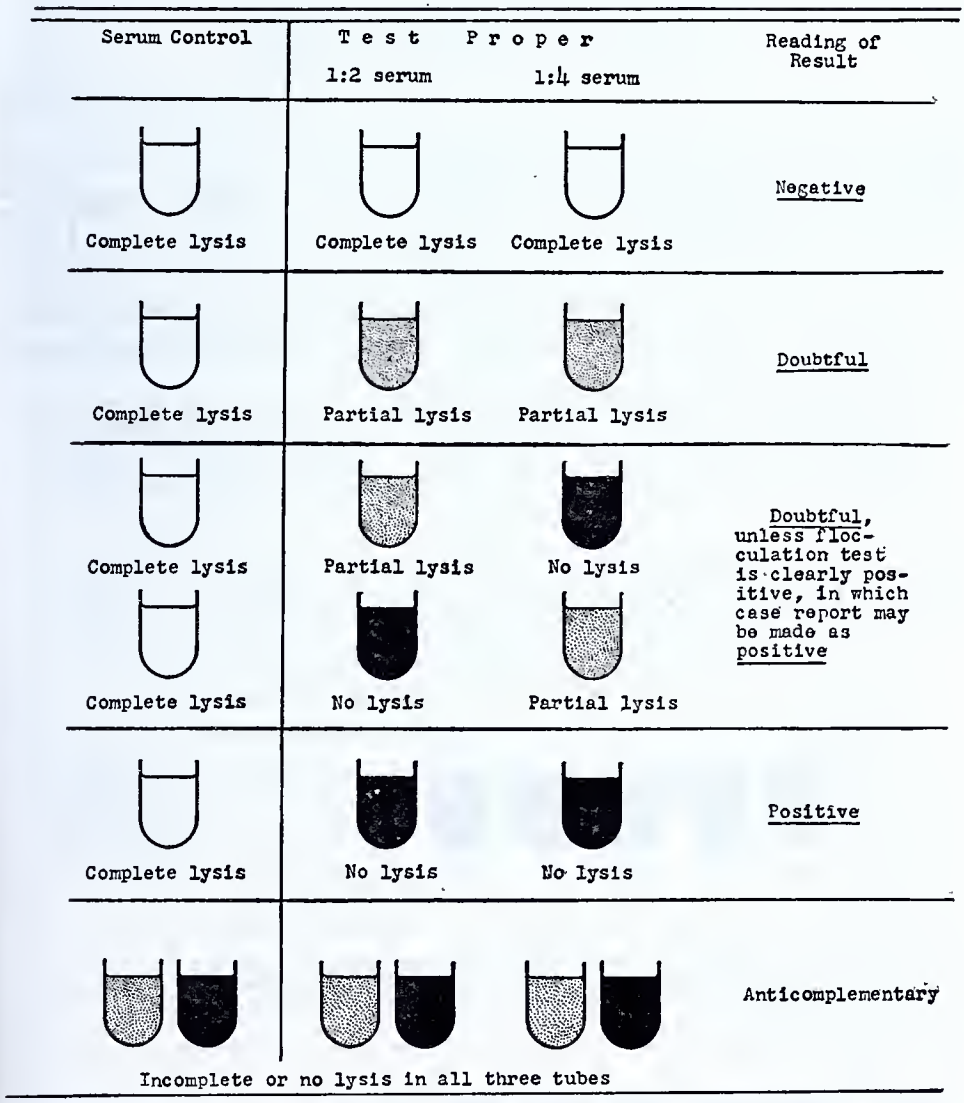

FIGURE 2.—Reading of results in routine Wassermann test.

or 1 percent cholesterol is not demonstrably anticomplementary under the conditions of the test. Failure to hemolyze indicates that the complement is defective and is deteriorating under the conditions of the test.

(*b*) *The complement controls* incubated along with the tests should show approximately the same degree of hemolysis as the first set used to check the amboceptor titration. Any pronounced differences, illus-

trated in the accompanying table, indicate either that the complement is defective and is deteriorating under the conditions of the test, or that the antigen is significantly anticomplementary under the conditions of the test. Such deterioration with fresh complement indicates that the guinea pigs are in poor condition, and necessitates the greatest caution in the reading of results.

Example of complement deterioration

	Tube 1	Tube 2	Tube 3	Tube 4
Amount of complement referred to that used in the test.	Same	½	⅓	¼
Hemolysis caused by freshly prepared dilutions	Complete	Complete	Partial	Trace
Hemolysis caused after storage at 0°–5° C. for 4 hours, followed by ½ hour at 37° C.	Almost complete	Trace	Trace	None

(*c*) *Reading of tests proper.*—Figures 2 and 3 are reproduced from the Laboratory Diagnosis of Syphilis (*1*) and illustrate the reading of

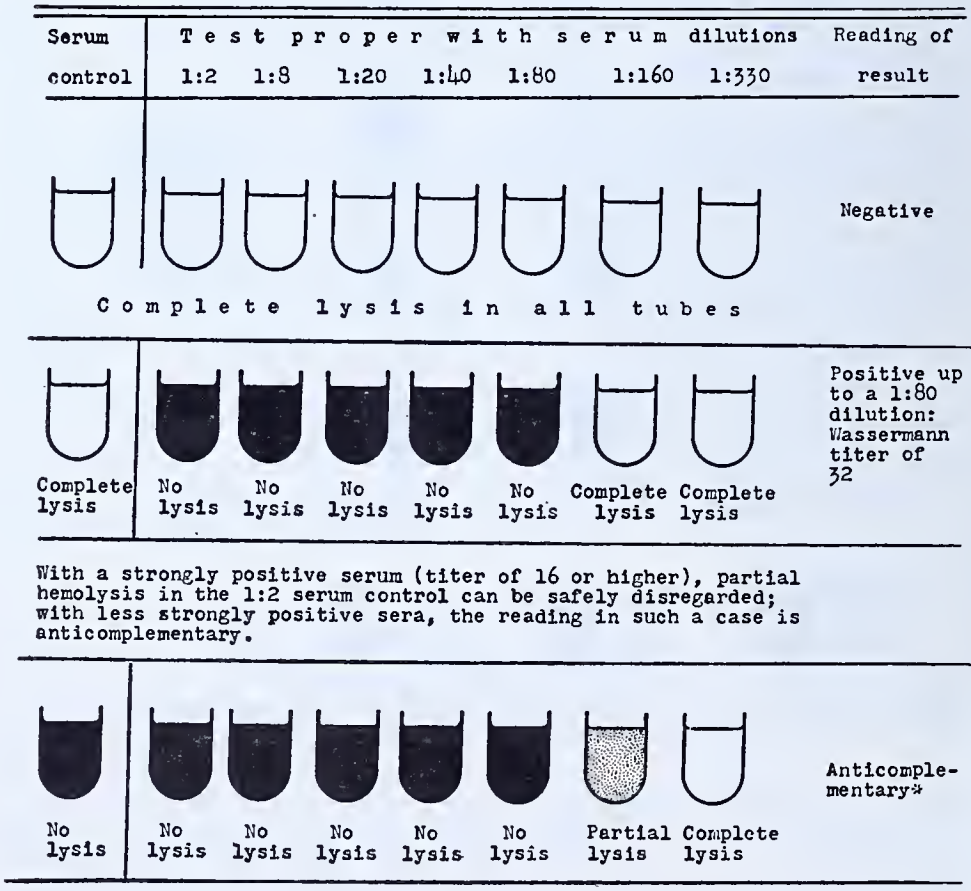

FIGURE 3.—Reading of quantitative serum tests.

results. They are self-explanatory. If the serum as such destroys complement, in the absence of antigen, it is anticomplementary—a

result which offers no evidence as to the presence or absence of syphilitic infection. If the serum control is completely hemolyzed, and the tubes of the test containing serum, complement, and antigen show no hemolysis, complement has been fixed by a lipoid-reagin compound, and the result is positive. If all three tubes show complete hemolysis, the complement has not been fixed and the result is negative. Finally, if the tests show partial hemolysis, the serum control being completely hemolyzed, only part of the complement has been fixed, and the result is doubtful.

In the quantitative Wassermann test the result is given as the maximum dilution of serum which continues to give a positive result. In figure 3, the serum may be said to be positive up to a 1:80 dilution. Similarly, in the spinal fluid test, a Wassermann positive fluid may be said to be positive down to, for example, 0.5 cc.

Table 6 is a condensed summary of the Wassermann test just described.

REFERENCES

(*1*) Eagle, Harry: Laboratory diagnosis of syphilis. St. Louis, The C. V. Mosby Company, 1937.

(*2*) Eagle, Harry: A new flocculation test for the serum diagnosis of syphilis. J. Lab. & Clin. Med., 1932, 17: 787.

(*3*) Eagle, Harry: Modifications in the technic and interpretation of the Wassermann reaction. J. Lab. & Clin. Med., 1933, 18: 821.

(*4*) Eagle, H.; Brand, A. F.: A micromodification of the flocculation technic. Am. J. Syph., Gonor. & Ven. Dis., 1938, 22: 22.

(*5*) Strauss, J. H.: Am. J. Syph., Gonor. & Ven. Dis., 1937, 21: 406.

TABLE 6.—*Outline of routine serum and spinal fluid Wassermann tests*

		Serum* or spinal fluid, cc.	0.85 per-cent salt solu-tion, cc.	Anti-gen dilu-tion, cc.	Com-ple-ment, 1:10, ce.		Sensi-tized sheep cells (1.5 per-cent), ee.		Example of read-ing of hemolysis	Result of test in the sample cited
Antigen control (no serum)		0	0.4	0.4	0.4	The entire series of tests are now placed at 3°–5° C. for 3 to 4 hours, followed by ½ hour at 37° C. Sensitized cells are then added as indicated in the next column.	0.8	The tests are now replaeed at 37° C. for 20–30 minutes, when the results are read. The tubes may be removed from the bath as soon as the second tube of the complement control is completely hemolyzed.	Complete	
Complement controls		0	.4	.4	.4		.8		Complete	Cells correctly sensitized with amhoceptor.
		0	.6	.4	.2		.8		Complete	
		0	.7	.4	.13		.8		Partial	
		0	.7	.4	.1		.8		Trace	
		0	.8	.4	.0		.8		None	
Routine serum test	Serum control	0.2	.6	0	.4		.8		Complete	Serum positive.
	Test proper	.2	*.2	.4	.4		.8		None	
		.1	*.3	.4	.4		.8		None	
Spinal fluid test	Spinal fluid	1.0	0	0	.2		.4		Complete	Spinal fluid positivo down to 0.2 cc.
	Controls†	.1	*.3	0	.2		.4		Complete	
	Test proper	1.0	0	.2	.2		.4		None	
		.6	0	.2	.2		.4		None	
		.4	0	.2	.2		.4		None	
		.2	0	.2	.2		.4		None	
		.1	*.1	.2	.2		.4		Partial	
		.05	*.15	.2	.2		.4		Complete	
		.025	.20	.2	.2		.4			

*The serum is inactivated; the spinal fluid is tested fresh.

†May be omitted.

THE HINTON[1] AND DAVIES-HINTON TESTS FOR SYPHILIS

WILLIAM A. HINTON, M. D., and JOHN A. V. DAVIES, M. D.

INTRODUCTION

In the detection of syphilis the Hinton and Davies-Hinton tests are of special value because of (1) the volume of output by the regular method; (2) quick results in emergencies by the rapid method; (3) the small amounts of blood required by the Davies-Hinton microflocculation test; (4) easy examination of spinal fluids by the Davies-Hinton test.

HINTON TEST FOR SYPHILIS. THIRD MODIFICATION

This test requires precision in execution because consistently accurate results cannot be obtained if minor variations in technic are allowed.

EQUIPMENT

1. Test tube racks. To simplify numbering and pipetting serums, these racks should be constructed to hold 10 or 20 tubes in a row.
2. Serum tubes 100 mm. long, with an approximately uniform inside diameter of 11 mm.
3. A water bath for inactivating serums (uncovered).
4. A Wassermann bath (uncovered). The water in the bath should be changed frequently to prevent a deposit from sticking to the outside of the tubes.
5. A centrifuge with a speed of over 2,000 revolutions per minute.
6. A maximum and minimum thermometer.
7. Graduated 100-cc. and 250-cc. cylinders to measure the reagents.
8. Dropping pipettes with rubber bulbs of about 5 cc. capacity for drawing off serums.
9. Serologic pipettes of 1.0 cc. capacity, graduated in tenths to the tip, to measure serums, and 5-cc. or 10-cc, serologic pipettes to measure reagents.

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[1] The reliability of this test in comparison with others is authoritatively shown in a series of papers by the American Committee on the Evaluation of Serodiagnostic Tests for Syphilis. This committee has acted impartially. Nevertheless, its figures and statements have been subject to biased interpretations by individual writers. Therefore, a careful study of these original reports is highly desirable in selecting serologic tests for syphilis. (*1, 2, 3, 4.*)

All inuiries regarding this test sould be addressed to Dr. W. A. Hinton, Boston Dispensary, 25 Bennet St., Boston, Mass.

10. Thick-walled Erlenmeyer flasks (*5*) of 125-cc. or 250-cc. capacity, with an inverted V-shaped ridge blown in the bottom, for mixing glycerinated indicator. This ridge produces two semicircular compartments, each of which holds 3 to 5 cc. These flasks (fig. 1) are not listed in any of the catalogues; ours are especially made by Macalaster Bicknell Co. of Cambridge, Mass.

PREPARATION OF STOCK SOLUTIONS

Stock indicator.—Extract dried, ground, beef-heart muscle (Bacto beef heart, dehydrated, Difco Laboratories) by putting 100 grams [2] of the powder and 400 cc. of anesthesia ether in a wide-mouthed glass-stoppered bottle and shaking thoroughly by hand for 10 minutes. Allow the bottle to stand 5 to 10 minutes so that the solid material may settle out. Then pour as much of the ether as possible through filter paper into an Erlenmeyer flask without pouring out any large quantity of the solid material. Scrape the solid material from the filter paper into the bottle for further extractions. Do not allow the main portion of extracted tissue to dry between extractions. Discard the ether filtrate in the Erlenmeyer flask. Make five separate extractions in all, using 400 cc. of fresh ether and a new filter paper for each. After the final extraction let the tissue dry on the filter paper. Obtain the net weight of this dried residue of ether-insoluble constituents. Place this dried residue in a glass-stoppered bottle with 95 percent ethyl alcohol, using 5 cc. of alcohol to each gram of residue. Extract for 3 days at room temperature (17° to 20° C.), shaking the contents of the bottle vigorously by hand for 5 minutes three times each day. Remove the solid material by filtering into a graduated cylinder; measure the alcoholic extract and transfer to a glass-stoppered bottle. Add cholesterol (using 0.4 gm. to each 100 cc.) and warm at 37° C. in an incubator or water bath, occasionally shaking, until the cholesterol has dissolved. A solution thus prepared is called stock indicator (antigen).

Reliable results can be assured only if a stock indicator prepared according to the above directions has proved to be accurate in comparative tests with an indicator that is known to be wholly satisfactory as determined by both clinical and serologic means. Materials designated for this test by the Difco Laboratories of Detroit, Mich., have met this critical requirement.

The stock indicator should not be stored in a refrigerator, for chilling will precipitate the cholesterol; if, by inadvertent chilling, the cholesterol should precipitate, it must be redissolved (by heating in a water bath at 37° C.). Stock

[2] The extraction in one operation of larger or smaller amounts of the powder has appeared to yield an inferior reagent.

FIGURE 1.

indicator kept in colorless, glass-stoppered bottles at room temperature for more than 2 years has given as good results as that freshly prepared.

Five percent salt solution.—Prepare a 5 percent solution of sodium chloride (C. P.) in sterile distilled water, and add 1.0 gm. of salicylic acid (C. P.) to each 4,500 cc.

The salicylic acid helps to preserve the potency of glycerinated indicator (described later).

Fifty percent solution of glycerol.—Prepare by mixing equal volumes of Baker & Adamson's Glycerin (Reagent)[3] and sterile distilled water.

The 5 percent salt solution and the 50 percent glycerol solution keep indefinitely.

Glycerinated indicator.—These directions for mixing glycerinated indicator should be followed strictly. Thirty cc. is the smallest and 150 cc. the largest amount that can be prepared satisfactorily at one time. If larger quantities are desired, two or more batches should be pooled.

The technic of preparing the glycerinated indicator is as follows:

Pipette one part of cholesterinized heart extract (stock indicator) into one compartment of the Erlenmeyer flask (with the inverted V-shaped ridge), and 0.8 part of the 5 percent salt solution in the other. Use great care in pipetting the salt solution into the flask in order to avoid premature mixture of the two solutions.

Mix by shaking the flask very rapidly from side to side for one minute. Let the mixture stand exactly 5 minutes.

Without further delay add 13.2 parts of the 5 percent salt solution and again shake thoroughly.

Finally, add 15 parts of the 50 percent glycerol solution and shake until the suspension is homogeneous. This mixture is called *glycerinated indicator.* If stored in a glass-stoppered bottle and kept continuously in a refrigerator at a temperature of about 8° C., it will remain unimpaired in strength for at least a month. For this reason some laboratories may wish to prepare enough for more than a day's testing. If this is done, the stock bottle of glycerinated indicator should be well shaken and the amount required for the tests at hand should be poured into another receptacle and the stock bottle of glycerinated indicator returned immediately to the refrigerator. Exposure to ordinary room temperature for more than a few minutes may seriously decrease its potency.

This stability of the glycerinated indicator under appropriate conditions of storage has these advantages:

1. It affords an indicator at all times for rapid tests.
2. It eliminates the frequent preparation of indicator, which is helpful if only a few tests are done at a time.

PERFORMING THE TESTS

1. Centrifuge the blood, if necessary, to aid in separating the serum from its clot; with a long dropping pipette remove the serum (free

[3] This is an especially pure redistilled glycerin.

from blood cells) and deliver into an appropriately labeled serum tube.

To avoid contamination of one serum by another, after each serum has been drawn off, thoroughly rinse the dropping pipette at least three times with sterilized physiologic salt solution. To minimize bacterial contamination, after every 20 serums have been drawn off empty the washing bottle (about 200 cc. capacity) and fill it with fresh salt solution.

2. Heat the serums in the inactivating bath at 55° C. for 30 minutes. Be sure that the level of the water is above the level of every serum and that the temperature is kept at 55° C. or 56° C. throughout inactivation. Serums should not be inactivated before the day of testing. If it is necessary to retest a specimen, use serum freshly separated from the clot.

3. Select all serums that show (*a*) hemolysis, manifested by redness greater than is produced when 0.1 cc. of blood is dissolved in 3.0 cc. of distilled water; (*b*) bacterial contamination, shown by cloudiness; or (*c*) marked opacity from other causes. Place in a separate rack and test, as soon as possible, according to the rapid method (p. 22). This will avoid further deterioration, which by decreasing the sensitiveness of the test and increasing the opacity of the medium makes the test harder to read.

4. Set up the racks with one properly numbered serum tube for each remaining specimen. Tubes should be clear and clean.[4]

5. With a 1.0-cc. pipette, measure 0.5 cc. of each heated (inactivated) serum into the tube that has been labeled for it. (Use a separate pipette for each serum.)

For routine purposes 1 tube is sufficient for each test. If, however, this test is negative and there is reason to suspect syphilis, it is desirable to retest the specimen using 0.1 cc. in 1 tube and 0.5 cc. in the other. We have found that in approximately 1 syphilitic out of 200, the second tube, containing the 0.1-cc. of serum, gives a positive reaction, while the first, which contains the 0.5-cc. of serum, gives a negative reaction.

If less than 10 tests are to be made at 1 time, use positive and negative controls.

6. Compare the appearance of each pipetted serum with that in the tube from which it was taken. This is to make sure that there has been no error in pipetting or in labeling the tubes.

7. Not more than 30 minutes before incubation, add with a clean 10-cc. pipette 0.5 cc. of glycerinated indicator to each serum.

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[4] To clean the tubes, rinse them thoroughly as soon after use as possible with tap water, and then fill each with a warm solution of 5 gm. of sodium hydroxide in 1,000 cc. of tap water; allow them to stay in this solution for about 2 hours and wash thoroughly with hot water to remove the alkali. This process usually removes (without the aid of a test-tube brush) any deposit which may have remained from previous use.

8. Pipette 0.5 cc. of the same indicator and 0.5 cc. of the 5-percent salt solution into an empty serum tube. This serves as a control, the use of which will be indicated later (p. 22).

9. Incline the rack to an angle of about 45° and then shake by thrusting it quickly upward and forward, then downward and backward with sufficient speed to cause the fluid to travel halfway up the tubes and make small bubbles. At least 3 minutes of shaking are required for accurate results. If there are enough tests, a shaking machine is desirable.

10. Place the rack in the Wassermann bath at 37° C. and let it remain for 16 hours (conveniently from 5 p. m. to 9 a. m.). Longer incubation makes the tests increasingly hard to read. Do not agitate the tubes before reading.

When the racks containing the tests are removed from the bath, record the readings shown by the bath thermometer as well as those of the maximum and minimum thermometer. The temperature should not fall below 34° nor rise above 39° C.

Reading the results.—The tests should be read within an hour after the incubation has ended. To read them, sit in front of a window but do not face the sunlight. (The light must be good, and for this reason suitable artificial light must be provided on dark days or at night.) In order to determine whether or not there is clearing of the fluid and a ring or band of white flakes or white coarse granules at the meniscus, lift each tube carefully from the rack and hold it at the level of the eye; slant it at an angle of about 45° and view it in the direction of a darkened background on either side of a window or of a suitably placed light. While still viewing it at the same angle, slowly roll the tube between the fingers; this will make a faint ring visible. Finally, gently shake the tube and look for flocculation, evidenced by agglutinated masses or by faint granularity.

The reactions are read and reported as positive (without indicating the intensity of the reaction), negative, doubtful, and unsatisfactory.

Such reports do not confuse physicians by implying that the intensity of the reaction is related to the clinical condition of the patient (*6*).

Positive reactions (*recorded*+).—At or a little above the level of the meniscus there is a ring or band, approximately 0.2 to 1.5 mm. wide, of white coarse granules or flakes of lipoids, slightly to moderately but not strongly adherent to the wall of the tube.[5] By gentle shaking, the ring or band is loosened and the particles scattered so that they are visible as agglutinated masses in a clear fluid or as somewhat coarse granules in a cloudy field.

[5] Hemolyzed serums that are also bacterially contaminated frequently produce a whitish ring which is strongly adherent to the tube.

Negative reactions (*recorded* −).—Usually there is at most only slight clearing but no ring, band, or floccules. However, with some indicators, the negatives may show a "scummy" nongranular deposit of lipoids on the wall of the tube extending from the meniscus downward for from 1 to 3 mm.

Doubtful reactions (*recorded* ±).—Centrifuge for 10 minutes at high speed (about 2,000 revolutions a minute) (1) those tubes which on gentle shaking showed only slight granularity beyond that observed in the control tube (containing 0.5 cc. of indicator and 0.5 cc. of the 5 percent salt solution) and (2) those tubes which showed only a slightly flaky or slightly granular ring. If, as a result of the centrifuging, there is definite clearing, and on top a thin layer of lipoids which shaking breaks up into fine flakes or coarse granules, the test is recorded as ± and reported as doubtful; if these changes have not taken place, it is reported as negative.

RAPID METHOD

This procedure may be used whenever there is urgent need for a quick report, for example, in testing donors for transfusion and as an aid in the diagnosis of suspected primary and secondary syphilis. Although this method has not been officially evaluated it is, according to our experience, from 98 percent to 99 percent as accurate as the regular method. Because of this slight margin of error, it is recommended that the results be checked by the regular method on part of the serum whenever possible. It is our custom to test all specimens selected under number 3, page 20, by the rapid method.

TECHNIC OF RAPID METHOD

Heat the serums for 3 minutes at 60° C. Pipette 0.5 cc. of the serum into a serum tube and add 0.5 cc. of the glycerinated indicator; shake according to direction 9, page 21; place in the Wassermann bath at 37° C. for 20 minutes; centrifuge at about 2,000 r. p. m. for 10 minutes; read and record as follows:

Positive (*recorded* +) if there are plainly visible flakes at the top of the fluid, and a well-marked flocculate (precipitate) is seen on shaking.

Negative (*recorded* −) if centrifuging has caused no change, provided the specimen shows no decided hemolysis (see under 3, p. 20), or no marked bacterial contamination.

Unsatisfactory if the specimen is hemolyzed or bacterially contaminated, unless the reaction is strongly positive. This interpretation is necessary, because even the moderately hemolyzed or bacterially contaminated serum of a known syphilitic usually gives a negative reaction.

DAVIES-HINTON MICROFLOCCULATION TEST[6]

In order to facilitate carrying out this test (*7*), specimens of blood should be collected in special rubber-capped glass collection tubes (*8*) which are then placed in labeled glass tubes that measure approximately 100 mm. in length and 15 mm. in diameter, such tubes being ordinarily called Wassermann tubes. The collection tubes are made of ordinary glass tubing and measure 80 mm. in length by about 2.5 mm. in inside diameter. Over each end there should be a flexible rubber cap such as is used to stopper small bottles of vaccine or serum.[7] The capacity of the tube is about 0.3 cc.

LABORATORY PROCEDURE

Number the Wassermann tubes containing the specimens and place them in a serologic rack. Take each specimen in its collection tube from the rack, remove the rubber cap from one end, and loosen the clot from the wall of the tube with the stylet of an 18-gage needle or with some other stiff wire. Replace the rubber cap on the collection tube and return it to the numbered Wassermann tube; centrifuge at high speed for 10 minutes. Examine each specimen so handled to see if the serum is clear and well separated from its clot; if the serum is not clear, recentrifuge for another 10 minutes. If this still does not clear it, make a note of the condition of the serum. Place the rack containing the clear specimens (clot downwards) in a serologic water bath kept at 56° C., preferably for 30 minutes, or if in a hurry 20 minutes, having first filled the Wassermann tubes with water from the water bath. Next, remove the rack from the water bath, pour the water from the tubes, remove the cap from the serum end of each collection tube and notch it just above the junction of clot and serum with a file. Hold the collection tube horizontally, break it, and discard the part of the tube that contains the clot. Proceed with the part containing the clear serum as follows:

1. Drain into another glass collection tube enough serum so that the length of the column of serum is about 2.5 cm., and drain into a second similar glass tube enough serum so that the column is 0.5 cm. to 1.0 cm. long.

2. With a capillary pipette, add to the first tube glycerinated Hinton indicator equal to the amount of serum in the tube as estimated by the combined length of the column of serum and indicator.

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[6] This test in its single official evaluation (*2*) in 1936 stood highest, and when done for the sake of comparison in our own laboratory in the 1937–38 evaluation, it was 100 percent specific and 0.5 percent more sensitive than the regular Hinton test.

[7] These rubber caps may be obtained from the West Company, 1117 Shackamaxon St., Philadelphia, Pa. Specify No. 3 vial stoppers in No. 68 stock.

Care should be taken not to allow air to separate the serum and Hinton indicator, which would prevent mixing.

The capillary pipette consists of a piece of glass tubing about 10 or 12 cm. long and 1 cm. in diameter. One end is tapered to a capillary tip about 1 mm. or less in diameter; the other end is capped with a rubber bulb. Provided no serum is drawn into the capillary pipette, it need not be rinsed between specimens.

3. To the second tube, with the same capillary pipette, add diluted Hinton indicator equal to 5 times the amount of the serum as estimated by the combined length of the column of serum and indicator.

4. Mix the serum and the Hinton indicator in each tube by tilting the liquid toward alternate ends of the tube 10 or 15 times.

5. Cap both ends of the two collection tubes, return one to the original numbered Wassermann tube and the other to a Wassermann tube correspondingly numbered, and place the rack in a 37° C. serologic bath for 16 hours, having first filled the Wassermann tubes with water from the bath.

A beaker of water, maintained at 37° C. in a bacteriologic incubator, may be used instead of the serologic bath. If speed is desired, the tests may be incubated for only 30 minutes without apparent loss of accuracy.

6. Remove the rack from the water bath and centrifuge the tubes for 5 minutes at approximately 2,000 revolutions per minute.

7. Read the results with a low-power objective of the microscope. The light should be cut down by lowering the condenser so that aggregates at the meniscus can be seen readily. Moreover, the stage of the microscope should be tilted at an angle of about 30° from the horizontal and the tube placed under the lens so that the meniscus is uppermost. Readings are designated as follows:

Positive, if there are definite, discrete, compact clumps at the meniscus in *either* tube. Gentle thumping of the tube may help float the clumps into view.

Doubtful, if there are a few small clumps at the meniscus. In such cases, the clumps should be broken up by thumping the tube with a finger and the tube recentrifuged for 3 minutes. The test is reported "doubtful" if small clumps are again visible at the meniscus and "positive" if large, compact clumps are present in either tube.

Negative, if there are no clumps at all. Amorphous, cloudy, granular material at the meniscus should be interpreted as negative.

Unsatisfactory, if badly hemolyzed or contaminated specimens give no marked flocculation in either tube.

The technic described above requires about 0.1 cc. of serum; smaller amounts of serum (0.05 cc. or more) may be handled in the same way in capillary tubes [8]

[8] Capillary tubes of these specifications may be obtained from Friedrich & Dimmock, Millville, N. J.

measuring 10 or 11 cm. in length and 1.25 to 1.5 mm. in inside diameter, except that the tubes are sealed with a small gas flame instead of rubber caps.

DAVIES-HINTON FLOCCULATION TEST OF CEREBROSPINAL FLUID *(9)*

Although this test has not been officially evaluated, it has, in our experience, proved to be far easier to perform and more efficient than the Wassermann (*10*) and those flocculation tests with which we have compared it. This test is now being used by the Massachusetts Department of Public Health.

Specimens of spinal fluid for this test should not be cloudy because of bacterial contamination, which is likely to give falsely negative tests, nor admixed with more than a trace of blood, because in rare instances an excess of blood can cause a false positive reaction. These facts must be borne in mind when interpreting the results, for even if the specimen has been cleared by centrifuging, these statements still hold.

The test requires the following materials:

1. *Glycerinated Hinton indicator* (see p. 19) which may be made in sufficient quantity to last a month, provided it is stored in the refrigerator at a temperature of 8° to 10° C.

2. *Hinton-negative human serum*, which may be obtained by pooling serums that remain after performing the routine serologic tests. Select for this pooling only Hinton-negative serums that are clear (without hemolysis) and that have been inactivated at 55° C. for 30 minutes. The rather remote possibility of a zonal effect may be ruled out by testing the pooled serum in the following amounts:

Tube 1.—0.5 cc. serum and 0.5 cc. Hinton indicator.

Tube 2.—0.1 cc. serum and 0.5 cc. Hinton indicator.

Tube 3.—0.1 cc. serum and 1.0 cc. Hinton indicator.

Tube 4.—0.1 cc. serum and 2.0 cc. Hinton indicator.

Do a "rapid test," which consists in shaking the four tubes containing the serum and Hinton indicator for 5 minutes, placing them in a serologic bath at 37° C. for 30 minutes, centrifuging them for 10 minutes at high speed (about 2,000 revolutions per minute) and then reading the results. If all the tubes are negative, as shown by the absence of floccules, the serum is suitable for testing spinal fluid. The pooled serum should then be passed through a Berkefeld "N" filter and collected under sterile conditions in rubber-stoppered bottles, so that each contains not more than 3 days' supply. These should be kept in a refrigerator at 8° to 10° C. Pooled serum should be kept no longer than 3 weeks and should be thrown away sooner if it becomes cloudy. Old serum is likely to give falsely negative reactions.

Laboratories that test only a few spinal fluids at a time may find it more convenient to prepare only enough serum for the day by select-

ing one or two clear Hinton-negative serums of that day and retesting by the "rapid method" in the four amounts as indicated above.

3. *Gum acacia, 20 percent*, which is prepared by diluting two parts of 30 percent gum acacia [9] with one part of physiologic salt solution. This solution of acacia should be kept in a refrigerator and discarded when it becomes cloudy. In order to avoid accidental contamination of a large amount of the gum acacia, 5 to 10 cc. lots (sufficient for not more than 1 week's testing) should be put into small bottles or test tubes, autoclaved at 15 pounds pressure for 15 minutes, and then rubber-stoppered with sterile precautions. A preliminary test should be made on a sample of the lot, as follows:

Tube 1.—0.6 cc. of physiologic salt solution, plus 0.1 cc. of 20 percent gum acacia, plus 0.2 cc. of Hinton indicator.

Tube 2.—0.6 cc. of physiologic salt solution, plus 0.1 cc. of 20 percent gum acacia, plus 0.6 cc. of Hinton indicator.

Mix well by shaking with the hand, incubate in a serologic bath at 37° C. for 30 minutes, centrifuge at approximately 2,000 revolutions per minute for 10 minutes, and read. If either of the above tests is positive, as shown by the formation of floccules, the entire lot of gum acacia should be discarded.

Performing the tests.—Mix the 20-percent gum acacia with the previously tested Hinton-negative human serum in equal parts; for example, if 10 spinal fluids are to be examined, 3 cc. of the serum and 3 cc. of the 20-percent gum acacia mixed together will suffice for these specimens.

Before setting up the tests proper, perform a "rapid test," as follows:

Tube 1.—0.6 cc. of physiologic salt solution, plus 0.2 cc. of the freshly mixed acacia serum, plus 0.2 cc. of Hinton indicator.

Tube 2.—0.6 cc. of physiologic salt solution, plus 0.2 cc. of the freshly mixed acacia serum, plus 0.6 cc. of Hinton indicator.

Shake the tubes thoroughly with the hand, incubate in a serologic bath at 37° C. for 30 minutes, centrifuge at high speed (approximately 2,000 revolutions per minute) for 5 minutes, and note the results. If floccules are present in either of the tubes, the mixture is unsuitable for use and the ingredients thereof should then be investigated separately. On the other hand, if both tubes show no floccules, one may proceed with the test, as follows:

In a suitable rack set up two tubes (one behind the other), measuring 11 mm. by 100 mm. for each spinal fluid, and two tubes for controls. Label each tube.

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[9] The gum acacia (containing 4.5 percent of sodium chloride) may be purchased from the Eli Lilly Co. in 100-cc. ampules.

1. Pipette 0.6 cc. of the first spinal fluid into the first tube of the first row and the same amount of it into the corresponding tube of the second, and continue in this way with each specimen of spinal fluid. Pipette 0.6 cc. of physiologic salt solution into each control tube.

2. Pipette 0.2 cc. of the acacia-serum mixture into each tube of the first row (including the control) and then pipette 0.2 cc. of Hinton indicator into these same tubes.

3. Into each tube of the second row, including the control, pipette 0.2 cc. of the acacia-serum mixture and then 0.6 cc. of Hinton indicator.

4. Thoroughly and vigorously, either by hand or with a shaking machine, shake the rack containing the tests so that the contents become completely homogenous.

5. Incubate the tests in a serologic bath at 37° C. for 16 hours, taking care that the water level is slightly above that of the contents of the tubes.

6. Centrifuge all of the tubes including the controls for 5 minutes at approximately 2,000 revolutions per minute; then read first the controls and then the tests in front of a window or a suitable artificial light. Hold the tube at the top with one hand and tap near the bottom with a finger of the other hand. By such a procedure any floccules at the meniscus are dispersed downward and are easily visible. If the controls show any floccules at all, all of the tests should be declared unsatisfactory; otherwise, report the results as follows:

Positive, if in *either* tube for a given specimen there are definitely visible floccules. Positive tubes should not be centrifuged a second time, because this may change the reaction to negative on truly positive specimens; but all others should be centrifuged twice. Why this is necessary we do not know.

Doubtful, if either of the tubes shows questionable flocculation which centrifuging a second 5 minutes does not amplify.

If the original ground-glass appearance persists in *both* tubes of a given specimen, they should be centrifuged a second time for 5 minutes, read again and reported as *negative* if the ground-glass appearance persists; otherwise, the result should be reported as positive or doubtful, depending upon the visibility of the floccules.

Unsatisfactory, if the tubes containing spinal fluid that was originally turbid from bacterial contamination show no clearly visible particles but a cloudiness that is distinctly greater than that in the control tube; or if the test is positive in the presence of contamination with more than a trace of blood.

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OUTLINE OF STANDARD KAHN TEST

With Appendix of Special Kahn Procedures

REUBEN L. KAHN, SC. D.

PREFACE

The following outline of technic of the Kahn procedures has been abstracted from "The Kahn Test—A Practical Guide" (Williams and Wilkins Co., Baltimore). The principles underlying these procedures, elaborate discussion of the various steps employed, as well as the technic of preparation and standardization of antigen, are presented in the above volume. In this outline is presented the standard Kahn test with serum and spinal fluid, with a discussion of the interpretation of the precipitation results obtained. The outline also presents the technic of special procedures.

I. Apparatus.
II. Reagents.
III. Standard Kahn Procedures:
    A. Standard (diagnostic) test with serum.
    B. Interpretation of results of standard test.
    C. Standard (diagnostic) test with spinal fluid.
IV. Special Kahn Procedures:
    A. Presumptive test with serum.
    B. Presumptive test with spinal fluid.
    C. Quantitative test with serum.
    D. Quantitative test with spinal fluid.
    E. Verification test with serum.
    F. Microflocculation and other procedures.

I. APPARATUS

The use of standard apparatus in the performances of the various procedures is essential for correct results.

1. *Test tubes* for performing test (with serum and spinal fluid) are 7.5 cm. in length and 1 cm. in inside diameter.

2. *Vials* (with straight wall and flat bottom) for preparing antigen suspension are 5.5 cm. in length and 1.5 cm. in inside diameter.

All inquiries regarding this test should be addressed to Dr. R. L. Kahn, University of Michigan Hospital, Dept. Clinical Laboratories, Ann Arbor, Mich.

3. *Pipettes*—

10 cc. graduated to 0.1 cc.
1 cc. graduated to 0.01 cc.
0.6 cc. (or 0.45 cc.) graduated to 0.15 cc.
0.5 cc. graduated to 0.025 cc. (antigen suspension pipette, *optional*).
0.25 cc. graduated to 0.0125 cc. (antigen suspension pipette, *optional*).
0.2 cc. graduated to 0.001 cc.

4. *The test-tube rack* is made of suitable material (sheet copper, bakelite, etc.) 3 inches wide, 11½ inches long, 2¾ inches high, and consists of 3 shelves, the upper and middle ones containing 3 rows of 10 holes, each approximately half an inch in diameter. The center row of holes is offset half an inch.

5. *Standard shaking apparatus* has a speed of 275 to 285 oscillations per minute, with a stroke of 1½ inches.

6. *Water bath (56° C.)*.—Centrifuge and centrifuge tubes are of standard type.

7. *Washing of glassware*.—Tubes and vials are rinsed twice in tap water and boiled for 15 minutes in soft water containing a mild soap such as Ivory flakes. Then they are rinsed thoroughly in soft water and placed in cleaning solution [1] for about 24 hours, after which they are rinsed three times in soft water and twice in distilled water. They are then inverted in wire baskets and dried thoroughly in an oven.

Pipettes are rinsed by forcing soft and distilled water through the bores. They are placed in cleaning solution overnight, after which they are rinsed thoroughly twice in soft water and twice in distilled water. The pipettes are then placed in a slanting position in a wire basket and dried thoroughly in an oven. If cleaning solution is not employed, the glassware will accumulate a layer of organic material.

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[1] Preparation of cleaning solution (dichromic acid).

Concentrated sulfuric acid	460 grams (252 cc.).
Water	300 cc.
Sodium dichromate	60 grams.

Procedure.—(1) Mix water and $Na_2Cr_2O_7$ until dissolved. (2) Add H_2SO_4 *very* slowly, stirring constantly until the $Na_2Cr_2O_7$ is reprecipitated. Great caution must be taken in adding the sulfuric acid to the sodium dichromate solution. The solution becomes intensely hot and may boil over.

The transfer of cleaning solution from one jar to another may be carried out by a siphon arrangement as follows: A rubber tube is attached to the suction arm of a water vacuum pump connected with a faucet. The far end of the rubber tube is lowered to the bottom of the jar which is to be emptied of cleaning solution. By starting a stream of water through the faucet, a vacuum is created within the rubber tubing and the cleaning solution is at once drawn up into the tubing. By detaching this tubing from the faucet and placing it in another jar, the acid will continue to flow into that jar. A thin, acid-resistant rubber tubing is employed for this purpose, making it possible to see readily the cleaning solution rising within the tube.

Some laboratories report good results by washing tubes and vials with "Calgonite." The tubes and vials are washed in hot distilled water containing 1 ounce "Calgonite" per 20 liters. This is followed by individual cleaning of each tube by a rotary brush and rinsing twice with soft water and twice with distilled water.

II. REAGENTS

1. *Standard Kahn Antigen.*—This antigen is employed in the performance of the standard (diagnostic) tests with serum and spinal fluid and in the quantitative tests with serum and spinal fluid, and, in special instances, also in microtests. The antigen is standardized to the degree of specificity and sensitivity required for the standard Kahn tests.

(A) Standard antigen maintains the same titer for many years and remains uniform in specificity and sensitivity provided the following precautions are taken:

(*a*) Only chemically clean and dry glass vessels should be used for storing antigen and these should be properly stoppered, as evaporation of alcohol from the antigen will not only cause a change in the sensitivity of the antigen, but may cause the separation of cholesterol.

(*b*) Antigen should be kept at room temperature—not in the ice box nor in the incubator. It should be stored in the dark, as in a cupboard. The antigen bottle in daily use might be kept in a mailing container to avoid undue exposure to light.

(*c*) Antigen should not come into contact with rubber or cork because both contain alcohol-soluble elements which affect specificity. Such stoppers should be covered with thin high-grade tinfoil.

2. *Serum.*—(*a*) It is essential that the serum employed in the test be entirely free from cells or particles of any kind, since these may give the impression of a precipitate in the completed test.

(*b*) It is important to adhere to sterile technic in obtaining blood from patients. The tube into which the blood is emptied should be chemically clean, dry, and sterile. If the tube is agitated before a clot is formed, there will be a tendency toward hemolysis. After a clot is formed, this tendency is reduced to a minimum.

(*c*) It is well to break up the blood clot with wooden applicators before centrifugation. The inner wall of the tube is encircled with the applicators so as to separate completely the adhering blood clot. If the clot is contracted, it may be removed before centrifugation. The same applicators should *never* be used for more than one specimen of blood.

(*d*) Ten to fifteen minutes centrifugation at 2,000 revolutions per minute is usually sufficient for the separation of the serum from the clot. If serum is not absolutely clear it should be recentrifugated.

(*e*) The clear supernatant serum is either poured off into a clean tube or is pipetted off with a serum-transfer bulb-capillary pipette. If the same pipette is used for removing serum from different blood specimens, it should be rinsed at least six times in each of two containers of fresh salt solution and completely drained before using.

(*f*) The clear serum should be heated for 30 minutes in a water bath at a temperature of 56° C. before performing the desired test. The temperature of the water bath should *not* be 54°, 55°, or 57° C.

(*g*) Serums should be tested as soon as possible after being heated. For uniformity, it is well to begin the performance of the tests within 5 to 10 minutes after the serums have been removed from the 56° C. water bath. Serums that have been heated 2 to 24 hours previously should be reheated for 10 minutes, when they are to be reexamined; if after 24 hours, they should be reheated for 15 minutes.

(*h*) Serums showing some hemolysis or containing chyle or bile do not affect the correctness of Kahn results. But if markedly hemolyzed or decomposed because of bacterial contamination, they are not fit for serologic tests.

3. *Physiologic salt solution.*—This solution consists of 0.9 percent sodium chloride in distilled water. The sodium chloride must be chemically pure and the solution filtered before using. Sterility is not essential, but if the solution is contaminated, it is not fit for use. It is well to prepare quantities of salt solution sufficient for periods not exceeding 2 weeks. This step will assure the use of relatively fresh salt solution.

III. STANDARD KAHN PROCEDURES

A. STANDARD (DIAGNOSTIC) TEST WITH SERUM

The standard test is a three-tube test, each tube containing a different proportion of serum and antigen suspension. Optimum precipitation is obtained when the concentration of antigen and antibody (reagin) approximate one another. Hence, it is well to employ a relatively large, moderate, and small quantity of antigen suspension with each serum, since the serum may contain a large, moderate, or small amount of antibody. The use of three proportions of serum to antigen suspension makes it possible to obtain highly sensitive precipitation results with standard antigen which is a moderately sensitive but highly specific antigen.

The following outline presents the general plan of the Standard Kahn reaction giving four different ranges in precipitation:

	Tube 1	Tube 2	Tube 3
Serum: antigen suspension-ratio	3:1	6:1	12:1
Antigen suspension, cc	0.05	0.025	0.0125
Serum, cc	.15	.15	.15
TYPES OF PRECIPITATION REACTIONS			
Negative in the 3 proportions	−	−	−
Positive in the 3 proportions	++++	++++	++++
Positive only with the smaller amounts of antigen suspension	−	++	++++
Positive only with the larger amounts of antigen suspension	++++	++	−

1. *Preliminary preparations for test.*—Proper coordination and sequence of the various steps of the test, in relation to the number of specimens to be examined, are important for maintaining a high level of accuracy and efficiency. The racks should be set up, the tubes numbered, and the pipettes ready for measuring antigen suspension and serum. Antigen suspension is prepared as needed; hence, the amount prepared must conform to the number of tests to be made.

2. *Heating of serum.*—The serum, after it has been heated for half an hour at 56° C., is examined for the presence of particles. If present, the serum is cleared by recentrifugation.

3. *Preparation of standard antigen suspension.*—This suspension is prepared shortly before the serums are taken from the 56° C. water bath. Antigen is mixed with salt solution according to the required titer. Thus, if the titer is 1 cc. antigen plus 1.2 cc. physiologic salt solution, the antigen is mixed as follows: (*a*) 1.2 cc. salt solution is measured into a chemically clean and dry standard antigen suspension vial; (*b*) 1 cc. antigen is measured (with a chemically clean and dry pipette) into a similar vial; (*c*) the salt solution is poured into the antigen, and as rapidly as possible (without waiting to drain the vial) the mixture is poured back and forth six times to insure thorough mixing; (*d*) the antigen suspension is allowed to stand for 10 minutes before using. The suspension is not to be used after standing a total of 30 minutes from the time of mixing. An old antigen suspension is not to be mixed with a newly prepared suspension.

More than 1 cc. of antigen may be mixed with a proportionately larger amount of salt solution. Thus, in case of an antigen with the above titer, 2 cc. may be mixed with 2.4 cc. salt solution and 2.5 cc. with 3.0 cc. salt solution. Do not use amounts of antigen less than 1 cc. nor more than 3 cc. for the preparation of an antigen suspension.

4. *Measuring antigen suspension.*—The antigen suspension is shaken well, and 0.05, 0.025, and 0.0125 cc. amounts are measured for each serum, delivering the suspension to the bottom of the tubes. The standard rack capacity is 30 tubes; 0.05 cc. amounts are measured into the tubes of the first row, 0.025 cc. amounts in the tubes of the second row, and 0.0125 cc. amounts in the tubes of the third row.

5. *Measuring serum.*—The serum is added as soon as possible after the antigen suspension has been pipetted to avoid undue evaporation of the suspension. When examining large numbers of serums, it is well for 1 worker to measure the antigen suspension and for another to follow with the serums. It is necessary to limit the tests to be performed to groups of 10. This number will permit the pipetting of antigen suspension and serum to be completed within 5 minutes. *It is of the utmost importance to use a clean, dry pipette for each*

serum. Each serum, in 0.15 cc. amounts, is added to the 0.05, 0.025, and 0.0125 cc. amounts of antigen suspension, and the rack of tubes is shaken vigorously for 10 seconds to insure thorough mixing of the ingredients. The serum-antigen mixtures should stand for about 5 minutes (preferably not less than 3 minutes and not more than 7 minutes) at room temperature before the mechanical shaking for 3 minutes (see 7 below).

6. *Controls.*—Set up four separate tests, one with a strongly positive serum, one with a weakly positive serum, one with a negative serum, and one employing salt solution (with antigen suspension) instead of serum. The antigen suspension for these controls should be pipetted immediately before pipetting the antigen suspension for the tests, and the serum for these controls, immediately before the serums for the tests have been pipetted.

7. *Shaking.*—The tests and controls are shaken in a standard shaking machine for 3 minutes. The machine oscillates 275 to 285 times per minute, with a stroke of 1½ inches.

8. *Addition of salt solution.*—After the 3-minute shaking period, 1 cc. salt solution is added to each tube of the first row of the rack (containing the 0.05 cc. amounts of antigen suspension) and 0.5 cc. salt solution to the remaining tubes. The rack is shaken by hand sufficiently to mix the ingredients.

9. *Time of reading results.*—Results are read immediately after the addition of salt solution and a check reading is made 15 minutes later, the racks remaining at room temperature during this interval. The final result is the average of the first and second readings.

B. INTERPRETATION OF RESULTS OF STANDARD TEST

1. *Methods of reading results.*—Optimum reading conditions in each laboratory should be determined by trial. The following points will be found helpful: (*a*) When utilizing daylight for reading the tests it is well to have but one source of light coming from a single window immediately in front of the reader. It will be found satisfactory to shade the upper and lower portions of the window, narrowing the source of light to a section several feet in height. Light from any other windows near the reader should be dimmed by lowering the window shades. (*b*) When holding the rack in front of the exposed section of the window, the definitely positive and the negative reactions may be readily differentiated without lifting the tubes from the rack. (*c*) In case of weak reactions each tube should be examined individually, lifting it several inches above the eye level and slanting it until the fluid is spread into a thin layer. The precipitate will then become readily visible.

Those preferring magnification will find the microscope mirror helpful. Place mirror on reading table with concave surface upward. Hold the tube in slanted position 2 to 3 inches above the mirror and examine the image in the mirror. Both daylight and artificial light may be employed. One may also utilize an ordinary hand lens for reading the tests. A two- or three-fold magnification will be found satisfactory. Some workers prefer the use of a slit-light arrangement, the source of light being an electric bulb enclosed in a box which is provided with a narrow slit.

As far as possible, workers should limit themselves to one method of reading. The occasional use of magnification by readers who usually do not resort to it will be likely to affect the uniformity of their reading scale. It should be emphasized that certain highly magnifying agglutinoscopes show particles in serum alone, and are thus unfit for use in this test. The magnification must be sufficiently low to assure opalescent and clear-cut negative reactions, with entire freedom from visible foreign particles.

2. *Interpretation of results.*—(*a*) Each of the three tubes of the test is read independently of the other tubes in the rack. In each tube, a definite precipitate suspended in a clear medium is read four plus. Proportionately weaker reactions are read three, two, and one plus and plus-minus or doubtful, respectively.

(*b*) Strongly potent serums show complete or four-plus precipitation in each of the three tubes, but, due to the different amounts of antigen suspension employed, the precipitates are unequal in bulk, being greater in the first tube and least in the last tube.

(*c*) Serums that are not strongly potent do not show complete precipitation in each of the three tubes. Such serums show most marked precipitation in the third tube because the small amount of antibody (reagin) reacts best with a small amount of antigen suspension. These serums generally show weak precipitation in the middle tube which contains a moderate amount of antigen suspension, and no precipitation in the first tube which contains a relatively large amount of the suspension.

(*d*) Another type of precipitation reaction is met with occasionally, namely, one in which precipitation is marked in the first tube, and weak or negative in the second or third tube. In this instance, the serum generally is so markedly rich in antibody that it requires a relative excess of antigen suspension to give maximum precipitation. When a reaction of this type is met with, it is necessary to set up a supplementary test in which the amount of antigen suspension in relation to serum is increased beyond that employed in the standard

test. A supplementary test is set up in which 2:1 and 1:1 proportions of serum to antigen suspension are used, thus:

	Tube 1	Tube 2
Antigen suspension, cc	0.025	0.025
Serum, cc	.025	.05
Shake tests, 3 minutes.		
Salt solution, cc	.3	.3

These two tubes, or at least tube 2, should show definite precipitation reactions if the serum is strongly positive.

As an additional check on serums giving precipitation reactions in the first tube of the standard test and negative reactions in the remaining two tubes, a second supplementary test is made by setting up a partial quantitative test. Thus, dilute the serum 1:5, 1:10, and 1:20 with salt solution and test each dilution with antigen suspension in a proportion of 15:1, in accordance with the following outline:

	Tube 1	Tube 2	Tube 3
Antigen suspension, cc	0.01	0.01	0.01
Diluted serum, cc	.15 (1:5)	.15 (1:10)	.15 (1:20)
Shake tests, 3 minutos.			
Salt solution, cc	0.5	0.5	0.5

If one or more tubes should show definite precipitation reactions the serum can be considered positive. (In our experience, one serum was so highly potent that it did not begin to show precipitation until the dilution was brought up to 1:60 with salt solution. Such serums, however, are extremely rare.)

If these supplementary examinations do not show positive reactions, then the three-tube test which shows marked precipitation in the first tube and negative precipitation in the remaining two tubes must be considered as giving a weak or doubtful reaction.

Rarely one finds that the three-tube tests show a border-line precipitate in each of the three tubes, such as ±, ±, ±; +, +, + or perhaps ++, ++, ++. After ascertaining that these border-line reactions are not due to a serum precipitate, the two supplementary tests described above are carried out. If these two tests show definite precipitation, the tests are reported as positive. If the supplementary tests are also border-line or questionable, the chances are one is dealing with nonspecific precipitation due to conditions other than syphilis.

3. *Recording results.*—A permanent record must be made of findings in all tubes of each test at the time of reading. All tests should

be read independently by two workers. When two workers are not available, the original reading should be checked by the same worker after an interval of 15 minutes.

4. *Reporting results to physicians.*—The following tables illustrate the method of reporting the reactions, based on the precipitation results in each of the three tubes of the standard Kahn test. In this laboratory, a first reading is made immediately after the addition of salt solution following the 3-minute shaking period, and a second reading is made after the racks have stood for 15 minutes at room temperature. The precipitation results listed in the tables represent the average of the two readings. This average is the same in the majority of instances—especially when the temperature at which the test is carried out closely approximates 21° C. (A ± reading is disregarded in averaging the results.)

TABLE 1.—*Types of reactions reported "Positive (++++)"*

	Tube 1	Tube 2	Tube 3
1	++++	++++	++++
2	+++	++++	++++
3	++++	++++	+++
4	++++	++++	++
5	++++	++++	+
6	++++	++++	−

Experience has shown that serums reacting as in 4, 5, or 6 are strongly positive.

TABLE 2.—*Types of reactions reported "Positive (+++)"*

	Tube 1	Tube 2	Tube 3
1	++	++++	++++
2	+	++++	++++
3	−	++++	++++
4	++	+++	+++

TABLE 3.—*Types of reactions reported "Positive (++++)" provided supplementary examinations 1 and 2 are "Positive." If supplementary examinations are negative, reactions 1 and 2 are reported "Positive (++)"; reactions 3–6, "Doubtful (+)"; reactions 7 and 8, "Negative"*

	Tube 1	Tube 2	Tube 3
1	++++	+++	−
2	++++	++	−
3	++++	+	−
4	++++	−	−
5	+++	−	−
6	++	++	++
7	+	+	+
8	±	±	±

TABLE 4.—*Types of reactions reported "Positive (++)"*

	Tube 1	Tube 2	Tube 3
1	−	++	++++
2	−	+	++++
3	−	+++	+++
4	−	++	+++
5	+	++	++

TABLE 5.—*Types of reactions reported "Doubtful (+)"*

	Tube 1	Tube 2	Tube 3
1	−	−	++++
2	−	−	+++
3	−	+	++
4	−	++	++

TABLE 6.—*Types of reactions reported "Doubtful (±)"*

	Tube 1	Tube 2	Tube 3
1	−	±	++
2	−	−	++

TABLE 7.—*Types of reactions reported "Negative (±)"*

	Tube 1	Tube 2	Tube 3
1	−	+	+
2	−	±	+

TABLE 8.—*Types of reactions reported "Negative"*

	Tube 1	Tube 2	Tube 3
1	−	−	−
2	−	−	+

5. *Repeat examinations.*—If the slightest doubt exists as to the correctness of results due to some error in technic or the character of the specimen, the test should be repeated; if no serum is available another specimen should be requested.

6. *General consideration with regard to reading.*—Some workers occasionally become so "sensitized" in reading results that they begin to see precipitates in tubes where no precipitates exist. Readers of tests should become thoroughly familiar with the general appearance not only of negative serum-antigen suspension mixtures, but of negative serum alone. Under conditions of sufficient magnification these will begin to show evidence of the presence of the very fine particles generally shown by colloidal solutions. The expert reader should be in a position to differentiate at once a specific precipitate from dust

particles, fibers or particles due to magnification. It should be emphasized that the use of scratched glassware in the test should be avoided. Such glassware often prevents the proper evaluation of the degree of precipitation.

C. STANDARD (DIAGNOSTIC) TEST WITH SPINAL FLUID

In this test, the spinal fluid globulins are precipitated by means of ammonium sulfate and redissolved in an amount of physiologic salt solution equivalent to one-tenth of the original spinal fluid volume. The concentrated globulin solution thus obtained is then tested with standard antigen suspension.

1. *Preparation of concentrated globulin solution—Reagents.*—The reagents needed for the preparation of concentrated globulin solution are (1) spinal fluid, (2) physiologic salt solution, and (3) a saturated solution of ammonium sulfate of the highest purity.

Procedure.—(*a*) Spinal fluid is centrifuged to render it free from cells and foreign particles.

(*b*) 1.5 cc. of the clear fluid is added to a standard Kahn test tube (7.5 by 1 cm.).

(*c*) To the same tube is added 1.5 cc. of a saturated solution of ammonium sulfate.

(*d*) The fluids are mixed by covering mouth of tube with thumb (protected with rubber) and shaking tube back and forth vigorously. The mixture is placed in a 56° C. water bath for 15 minutes to hasten the precipitation of the globulins.

(*e*) The mixture is centrifuged at high speed (about 2,000 r. p. m.) for 15 minutes to throw down the precipitated globulins completely.

(*f*) The supernatant fluid is removed as completely as possible with a finely drawn capillary pipette. An optional method for removing the supernatant fluid is to pour off the fluid and invert the tube in a standard rack over clean filter paper, allowing the moisture that adheres to the tube to drain and be absorbed by the paper for a period of 10 minutes. This draining period is not necessary if the inside of the tube is wiped dry by means of filter paper. The filter paper is first wound around a glass rod or pencil and is then inserted into the tube—without touching the precipitate. Fresh filter paper is employed for wiping each tube.

(*g*) Salt solution to the amount of 0.15 cc. is added to the precipitate which is redissolved readily by gentle shaking. In adding this salt solution, the point of the pipette is held close to the bottom of the tube to avoid washing down traces of ammonium sulfate that may adhere to the inner wall.

(*h*) This globulin solution is now examined for clarity and freedom from particles and is then ready to be tested with antigen suspension.

2. *Preparation of antigen suspension.*—Salt solution is mixed with antigen in the same manner as for the standard test with serum—according to the antigen titer required for spinal fluid. The antigen suspension is allowed to stand 10 minutes and must be used in the test within the next 20 minutes.

3. *Measuring antigen suspension.*—With a 0.2-cc. pipette graduated to 0.001 cc., 0.01 cc. of antigen suspension is measured to the bottom of a standard Kahn test tube.

4. *Measuring concentrated globulin solution.*—With another 0.2-cc. pipette, 0.15 cc. of the concentrated globulin solution is measured into the antigen suspension tube. Tests are shaken vigorously for 10 seconds to mix ingredients.

5. *Controls.*—Positive and negative spinal fluid controls are included.

6. *Shaking.*—After mixing the concentrated fluid with antigen suspension, the test is shaken at the standard speed for 4 minutes.

7. *Addition of salt solution.*—0.5 cc. physiologic salt solution is added to the tube.

8. *Reading results.*—Four-plus, three-plus, and two-plus reactions are reported as positive; one-plus reactions are reported as doubtful and plus-minus and negative reactions are reported negative. If the spinal fluid contains blood it should be so noted on the report.

9. *Check examinations.*—Each spinal fluid test should be performed in duplicate. Hence, the amount of spinal fluid required for a test is a little over 3 cc.

IV. SPECIAL KAHN PROCEDURES

A. PRESUMPTIVE TEST WITH SERUM

The presumptive test is an auxiliary method to the standard Kahn test. The main difference between the two methods is that the presumptive is more sensitive than the standard test. This increased sensitiveness is due to the fact that, in the presumptive test, sensitized antigen is employed which is more sensitive than standard antigen. The test was named presumptive because it may in isolated instances give false positives; hence, when employed for diagnosis, the reactions should be considered as presumptive in character. The presumptive test is of value (*a*) as a technical check on the standard test, (*b*) in treated cases of syphilis when a highly sensitive method is desired, (*c*) as an additional criterion in establishing the absence of syphilis.

Sensitized Kahn antigen.—This antigen is employed not only in the performance of the presumptive tests with serum and spinal fluid but also, in special instances, in the quantitative tests with serum and spinal fluid. Statements (*A*), (*a*), (*b*), and (*c*) on page 31 relative to standard antigen apply also to sensitized antigen.

The following outline gives the performance of the presumptive test with serum:

1. *Preparation of antigen suspension.*—(*a*) Measure 1 cc. of sensitized antigen into an antigen suspension vial. (*b*) Measure an amount of physiologic salt solution, indicated by the titer of the antigen, into a similar vial. (*c*) Pour the salt solution into the antigen vial and, as rapidly as possible, pour the mixture back and forth approximately six times. (*d*) Allow the antigen suspension to stand 10 minutes at room temperature before using. Set up control tests as outlined under "Standard Test with Serum," paragraph 6, page 34.

2. *Measuring antigen suspension.*—Measure 0.025 cc. of the thoroughly mixed antigen suspension into a standard tube (7.5 cm. in length, 1 cm. in diameter) with a pipette graduated in 0.025 cc. amounts, delivering the suspension to the bottom of the tube.

3. *Measuring serum.*—Add 0.15 cc. serum—after it has been heated for 30 minutes at 56° C.—and mix the serum with the antigen suspension by shaking the rack vigorously by hand for about 10 seconds.

4. *Shaking.*—Shake rack in the usual manner for 3 minutes in a shaking apparatus.

5. *Adding salt solution.*—Add 0.5 cc. physiologic salt solution to the tube and examine for presence of a precipitate.

6. *Interpretation of results.*—Complete precipitation, 4 plus or 3 plus, is interpreted as positive; a moderate precipitation reaction, 2 plus, is interpreted as doubtful, while very weak reactions, such as 1 plus or plus-minus, are classed with the negative reactions.

7. *Serum control.*—Examine each serum for foreign particles which might give the appearance of a specific precipitate. Particularly in the case of each positive reaction, it is essential to determine that the serum used in the test is free from foreign particles. In using the presumptive test as a check on the standard Kahn test, the same serum control is, of course, sufficient for both methods.

B. PRESUMPTIVE TEST WITH SPINAL FLUID

The presumptive test with spinal fluid is carried out exactly as the standard test, except that sensitized antigen is employed instead of standard antigen. With sensitized antigen, the spinal fluid test is more sensitive than with standard antigen and is believed to possess a relatively high degree of specificity.

In many laboratories, a spinal fluid test with sensitized antigen is employed routinely as a check on the spinal fluid test with standard antigen, although reports to physicians may be based on the results given only by the standard test.

C. QUANTITATIVE TEST WITH SERUM

The standard test is essentially qualitative in nature. When the reaction is positive no indication is obtained as to the relative potency of the serum. Two serums giving positive reactions may differ markedly in their potency. The extent of this difference may be readily determined by means of the quantitative test with serum. The test consists of two steps. Positive serums are first diluted, in series, with salt solution. Each serum dilution is then tested with standard antigen suspension. The highest dilution giving a positive precipitation reaction is the end point desired.

Some workers prefer the use of standard antigen in the quantitative test; others prefer the use of sensitized antigen. It is important to be consistent and to limit oneself to the use of either one or the other in reporting the test to physicians. Sensitized antigen will generally give quantitative results at a higher level than standard antigen, hence these antigens should not be confused in routine quantitative examinations.

1. *Dilution of positive serum with salt solution.*—A series of serum dilutions with physiologic salt solution is prepared so that the ratio of the volume of diluted serum to the volume of serum before dilution ranges from 5 (1 part serum plus 4 parts salt solution) to 60 (1 part serum plus 59 parts salt solution). The following scheme is employed:

Dilution number	Dilution ratio
(1)	1=0.2 cc. undiluted serum.
(2)	5=0.2 cc. undiluted plus 0.8 cc. salt solution.
(3)	10=0.7 cc. of (2) plus 0.7 cc. salt solution.
(4)	20=0.2 cc. of (3) plus 0.2 cc. salt solution.
(5)	30=0.2 cc. of (3) plus 0.4 cc. salt solution.
(6)	40=0.1 cc. of (3) plus 0.3 cc. salt solution.
(7)	50=0.1 cc. of (3) plus 0.4 cc. salt solution.
(8)	60=0.1 cc. of (3) plus 0.5 cc. salt solution.

Performance of test.—The serum dilutions being available, the antigen suspension is prepared in the usual manner. After 10 minutes standing, it is pipetted in 0.01-cc. amounts into each of 8 standard test tubes, depositing the suspension at the bottom of the tubes. With an appropriate pipette, 0.15-cc. amounts of the 7 serum dilutions are added in order, beginning with the highest dilution (8), to the tubes containing antigen suspension. The racks are shaken for 3 minutes in the usual manner, 0.5 cc. saline is added to each tube and the results are read.

3. *Determination of Kahn Units.*—A definite precipitate (++++, +++, or ++) is recorded as positive, while a very weak reaction is discounted. If a serum gives a ++++, +++, or ++ reaction

in an undiluted state only and is negative in the dilution series, it is considered as containing Kahn units as indicated by the plus-signs (4 units, 3 units, or 2 units, respectively). The potency of any serum which is positive on dilution is determined according to the formula S=4 D, where S is the serum potency in terms of Kahn units and D is the highest dilution ratio giving a positive (++++, +++, or ++) reaction. Thus, if serum dilution 1:5 is positive and 1:10 and higher dilutions are negative, the serum contains 5×4 or 20 Kahn units. If serum dilution 1:10 is positive and 1:20 and higher dilutions are negative, the serum contains 40 units.

4. *Reporting results.*—Results are reported "4 Kahn units," "40 Kahn units," etc., as the case may be.

5. *Highly potent serums.*—If a serum gives a positive precipitation reaction with a dilution ratio of 60, still higher dilutions of serum are examined with antigen suspension until a positive reaction is no longer obtained. Higher dilutions are readily prepared by resorting to tube 3 in the dilution series (1:10 dilution) of which an excess is prepared.

D. QUANTITATIVE TEST WITH SPINAL FLUID

This method consists in first establishing that a given spinal fluid is positive by the standard technic and then determining the potency of the spinal fluid by serial dilutions of the spinal fluid globulin with salt solution as in the case of the quantitative test with serum. Details of these dilutions and the interpretation of the results are given in "The Kahn Test—A Practical Guide." The tubes are shaken 4 minutes, 0.5 cc. of salt solution is added, and the results are read, and reported as in the case of the quantitative test with serum.

E. VERIFICATION TEST WITH SERUM

A procedure for the detection of false positive reactions has recently been developed. Two preliminary reports have appeared (University Hospital Bulletin, University of Michigan, Ann Arbor, 1940, 6:26; Archives of Dermatology and Syphilology, 1940, 41:817). In accordance with this procedure, a type of serologic reaction which is unrelated to syphilis, referred to as a general biologic type, is relatively widespread. It occurs among lower animals and, under various conditions, in man. Further studies are in progress.

F. MICROFLOCCULATION AND OTHER PROCEDURES

If there is insufficient serum for the regular three-tube test, the examination and report are made as follows:

1. If 0.21 cc. of serum is available, a three-tube test is performed, employing smaller quantities of serum and antigen suspension than in

the standard test, but maintaining the same 3:1, 6:1, and 12:1 proportions of serum-antigen suspension. Thus, 0.01 cc. standard antigen is measured into each of three tubes, and 0.03 cc., 0.06 cc., and 0.12 cc. serum are added, respectively, after which the steps of the diagnostic test are followed except that only 4 to 5 drops of salt solution are added to the completed test before the reading is made.

2. If less than 0.21 cc. serum is available, a one-tube test (microflocculation test) is made by employing 10 parts of serum to 1 part of antigen suspension. Thus, if 0.1 cc. of serum is available, it is employed with 0.01 cc. of antigen suspension; if 0.05 cc. serum is available, it is employed with 0.005 cc. of anigen suspension. These reactions are reported as microflocculation tests.

3. Dependable serologic results may be obtained with fluid from chancres and other syphilitic lesions. After cleansing the area with physiologic salt solution, and under moderate pressure, fluid from chancres or other lesions is collected by means of a fine capillary pipette. This is deposited at the bottom of a small agglutination tube and centrifuged to throw down cellular material. The clear supernatant fluid is mixed with standard antigen suspension in the proportion of 10:1. If 0.03 cc. of fluid is available, it is mixed with 0.003 cc. of antigen suspension. The tests are shaken for 3 minutes and two drops of salt solution are added before reading the results. A definite precipitate is read "positive," while freedom from a precipitate is read "negative." If it is desired to make a Kahn test with aqueous humor, it is necessary to employ the same technic as for the spinal fluid test. The aqueous humor is treated with an equal amount of saturated solution of ammonium sulfate and a test is made with the globulin concentrate.

MICROSCOPIC SLIDE PRECIPITATION TESTS FOR THE DIAGNOSIS AND EXCLUSION OF SYPHILIS *(1)*

B. S. Kline, M. D.

MATERIALS FOR THE SLIDE TEST

Serums.—These are prepared as for the complement fixation test, care being exercised that they contain no red blood cells or foreign particles. (They are heated at 56° C. for 30 minutes). In retesting serum within several days, reheating is unnecessary if the specimens have been kept at 8° to 12° C.

When blood is obtainable in small quantity only it is advisable to collect this in a narrow test tube (about 8 to 9 mm.) and to handle it in the same manner as a larger sample from the vein.

When blood is obtainable in very small quantity only it is advisable to collect this in a narrow glass tube with a capillary end. The end is then sealed, a narrow rod is passed through the open end to free the clot from the wall, and after the tube is centrifuged at high speed it is placed in a water bath at 56° C. with water above the upper level of the serum. After heating, the tube is filed and broken just above the clot and the serum allowed to run into or is drawn into a 1-cc pipette, graduated in hundredths.

For testing blood donors, immediately before transfusion especially, the serums may be heated at 61° to 62° C. for 4 minutes in place of at 56° C. for 30 minutes. It has likewise been found that serum heated for 15 minutes at 56° C. gives results practically identical with those with serums heated for 30 minutes at this temperature (*2*).

Glassware.—Microscope slides 2 x 3 inches as purchased are rubbed on both sides with Bon Ami paste (prepared by breaking up a cake of Bon Ami in a small quantity of hot water.) As soon as the paste is dry (in about 5 minutes) it is completely removed from the slide with a soft muslin cloth. For convenience the slides covered with paste may be stuck to each other, allowed to dry, and cleaned at any time.

Upon clean slides for the heated serum tests, 12 paraffin rings, each with an inside diameter of 14 mm. are mounted. (Inasmuch as the slide test results are influenced by the surface area of the chambers it is important that the paraffin rings be thin ones. With a little

All inquiries regarding this test should be addressed to Dr. B. S. Kline, Mount Sinai Hospital, Cleveland, Ohio.

practice the required amount of paraffin can be ascertained. At first, it may be difficult to make complete rings. These incomplete rings may be completed by applying the loop a second time to the open areas.)

For the spinal fluid tests double ring slides are prepared as follows: Upon the clean slide a steel mold $3\frac{3}{16}$ x $2\frac{3}{16}$ x $\frac{1}{8}$ inches with two central wells $1\frac{9}{16}$ inches in diameter is placed. A metal disk $1\frac{5}{16}$ inches in diameter and $\frac{3}{16}$ of an inch thick is then placed in the center of each well. The space between them is filled with hot wax (2 parts ordinary vaseline and 1 part parowax) from a 10-cc. glass syringe. After the mixture cools a few minutes, each disk is elevated from the slide and separated from the wax wall by turning the central screw handle a few times to the right (holding mold down at edge). After the disk is freed, it is lifted out. The mold is removed by inserting a thin blade between it and the slide.

On properly cleaned glassware, serum will flow to the boundaries of the chambers. If the serum balls up, the slide is not clean and is not satisfactory. Preliminary tests indicate that the Clay-Adams concavity agglutination slide is satisfactory for use in performing slide tests.

Pipettes.—The pipettes needed for delivering serums and spinal fluid, and those for preparing the antigen emulsions are the ordinary finely graduated 0.2 to 10 cc. pipettes. The pipette for the 1-percent acetic acid solution is a 0.2-cc. pipette graduated in 0.001 cc. The pipettes for delivering the antigen emulsions are Wright pipettes made from glass tubing 6 to 10 mm. in diameter with the tubes about 0.5 mm. in outside diameter, delivering a drop equal to about 0.008 cc. (62 drops per 0.5 cc.).

It is advisable to draw out the capillary pipettes so that one tube is slightly thicker than the other. The diagnostic emulsion should be dropped from the thicker tube, the exclusion emulsion from the finer tube. Emulsions may be dropped from a pipette or an open syringe through a No. 26 needle.

Instrument for making paraffin rings.—This is essentially the instrument proposed by Green (*3*). A piece of soft iron wire (No. 28) is wound twice tightly about a test tube (about 15 mm. in outside diameter) forming a double loop and leaving a double shaft about an inch in length. The two shafts are then twisted together to within a quarter of an inch of the free end. After removing the looped wire from the test tube, a piece of linen thread (No. 12) is started from the free end of the shaft after being fastened here by a single twist of the free ends. Three long turns are made reaching the loop which is then tightly wound with the thread. The winding is continued up the shaft to the free end where it is fastened between the two ends of the

wire by twisting them. The loop is then bent at right angles to the shaft. It is then reshaped by working the loop against the bottom of the test tube mentioned above. The shaft is then inserted into the handle of a teasing needle or into a straight hemostatic forceps.

The paraffin rings are made by dipping the instrument into smoking paraffin (about 120° C.) draining quickly at one point and transferring the remainder to the glass slide.

Paraffin ring makers smaller or larger than standard should not be employed. If the paraffin is too hot, it will spread too much and the chambers will be too small. Care should be exercised also that the wire end of the loop is sufficiently long to prevent transfer of paraffin on the bottom of the wooden handle to the glass slide.

Slide holders (for 3- by 2-inch slides).—The slide holder is a wooden lid of a slide box (3½ by 6¾ by ½ inches) containing an easily fitting thin wooden shelf having a small handle at each end.

The lid of a slide box without a holder is less satisfactory. If less than three slides are rotated in the holder, it is advisable to use a small piece of adhesive tape to hold the one or two slides in place.

Salt solutions.—0.85 percent sodium chloride (C. P. or reagent, Merck) solution used in the tests is prepared with distilled water having a pH of about 6. (Such water gives a lilac color when one drop of chlorphenol red indicator (LaMotte) is added to 0.25 cc. of it in a small chamber). Distilled water having a pH of 5.2 or less gives a yellow color with this indicator and is not satisfactory.

One percent acetic acid.—(C. P. reagent.) It is advisable to use not less than 1 cc. of acid (delivered from a 1 or 2 cc. pipette) and accordingly 99 cc. of distilled water.

Water.—It is important to use distilled water obtained repeatedly from one satisfactory source if possible. Failure to use water of the proper pH may be responsible for unsatisfactory results.

Antigen.[1]—The purified antigen used in the microscopic slide precipitation tests for syphilis is prepared as follows:

Two hundred grams of dried heart powder (Difco) is placed in a 2-liter Erlenmeyer flask.

One liter of absolute ethyl alcohol (99+ percent) (Rossville Commercial Alcohol Corporation, Lawrenceville, Ind.) is added.

After the flask is stoppered with a cork covered with tinfoil, it is shaken vigorously by hand at intervals for 2 hours. Better still two wide-mouth bottles (Difco bottles for 1 pound beef heart powder) each with 100 grams of beef heart powder and 500 cc. of absolute ethyl alcohol (99+ percent) are shaken vigorously in a machine for

[1] Standard materials, including antigen for the microscopic slide precipitation tests for syphilis, may be obtained from the LaMotte Chemical Products Co., Towson, Baltimore, Md.

2 hours. (This short extraction removes much of the desired antigenic substance in the powder.)

The extract is filtered into a liter cylinder through good grade filter paper of medium texture (Schleicher and Schull No. 597, 38.5 cm.). It is important to use fat-free filter paper, otherwise some adventitious lipoid material present will be added to the extract.

During filtration the mixture is stirred with a glass or porcelain spatula or spoon and toward the end pressed with the cork until the powder is quite dry.

The extract (about 775 cc.) is placed in the refrigerator at 8° to 10° C. for 24 hours.

During this time a fairly heavy white precipitate settles out. This is filtered off and the filtrate in a large evaporating dish is concentrated on a water bath at 45° to 50° C. determined by a thermometer bulb within the extract. For convenience, the concentration of the extract may be started by leaving it in an air incubator at 50° C. until the following morning, and then completed by placing it on the water bath. During evaporation of the alcoholic extract an irregular festoon appears at the periphery. When the extract reaches the proper concentration the festoon disappears and the margin of the concentrated extract is sharp.

In a warm room the extract is now poured quickly into 500 cc. of acetone, C. P. (Coleman and Bell) at 50° C. in a large evaporating dish. Stir the acetone a few times with the spatula or spoon to distribute the extract.

The dish is then placed in an air incubator at 37° C. for 15 minutes after which the acetone is quickly decanted leaving a soft yellow-brown wax adherent to the side of the dish. (Longer periods of precipitation and precipitation at lower temperatures permit of precipitation of adventitious substances as well, and such antigens give more sensitive and less specific results.)

The dish is then placed on a water bath or in an air incubator at 50° C. until the little acetone remaining has evaporated (about 30 minutes).

The wax is then worked together with the glass or porcelain spoon and placed in a glass-stoppered bottle. Then 80 cc. of absolute ethyl alcohol (99+ percent) that has been kept in an air incubator at 50° to 56° C. for one-half hour or longer, is added, and after a few minutes shaking, the bottle is placed in an air incubator at 50° C. and shaken gently after 15 minutes and again after 30 minutes, when it is removed from the incubator and placed in the refrigerator at 8° to 10° C. for 45 minutes.

The solution is then filtered at room temperature and the filtrate is evaporated down at 45° to 50° C. resulting in a soft brown wax (antigen wax). The wax is weighed and to each gram in a glass-stop-

pered bottle, 10 cc. of absolute ethyl alcohol (99 + percent) at 50° to 56° C. is added. After the bottle is shaken for a few minutes it is placed in an air incubator at 50° C. for 30 minutes, and then shaken a few minutes.

The slightly turbid solution is then placed at 8° to 10° C. for about an hour and then filtered at room temperature. The resultant clear filtrate is the antigen, and contains about 8.75 percent of the alcohol-treated acetone-insoluble wax.

The average yield of antigen wax from one-half pound of beef heart powder is 3.5 to 4 grams. The discarded acetone-soluble lipoidal residue (impurities) ordinarily weighs at least three times this amount.

The antigen keeps best at room temperature hermetically sealed in glass containers. In small-necked glass-stoppered bottles (opened from time to time) kept at room temperature it shows no appreciable change in specificity or sensitivity for at least 6 months. (As stated above it is important to follow the steps outlined in minute detail. Too long a precipitation in acetone, precipitation at too low a temperature, and use of improper chemicals, for instance, result in waxes which contain some impurities that determine a sensitivity greater than standard.)

PREPARATION OF ANTIGEN EMULSIONS FOR DIAGNOSTIC AND EXCLUSION SLIDE TESTS OF HEATED SERUM

Formula.—0.85 cc. of distilled water (pH about 6) ; 1.0 cc. 1 percent cholesterin (C. P. Pfanstiehl) in absolute ethyl alcohol (99+ percent) (1 gram cholesterin in 100 cc. absolute alcohol) ;[2] 0.1 cc. antigen; 2.45 cc. 0.85 percent sodium chloride (C. P. or reagent, Merck) solution (pH about 6).

The technic of preparing the emulsion according to the above formula is as follows: Into a 1-ounce bottle the required amount of distilled water (pH about 6) is pipetted.

The bottle is held at an angle, and, pipetting with the left hand, the 1-percent cholesterin in absolute ethyl alcohol (99+ percent) is allowed to run along the side of the neck of the bottle. At the same time the container is shaken or rotated fairly vigorously.

The bottle is then gently rotated from the neck for 20 seconds.

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[2] The 1-percent cholesterin solution for the emulsions is prepared in about 45 minutes by placing the cholesterin flakes and absolute alcohol in a glass-stoppered bottle in an oven or water bath at 50° to 56° C. and shaking gently a few minutes at 15 minute intervals. The solution kept in the incubator at 37° C. is thoroughly satisfactory for use as long as 2 months.

The sensitivity of an emulsion is greatly influenced by the quantity of cholesterin present. The sensitivity is likewise influenced by the quality of the cholesterin used. The cholesterin (Pfanstiehl. C. P.) that has been found uniformly satisfactory in the slide tests is flaky, pearly, and readily soluble to 1 percent in absolute ethyl alcohol (99+ percent). Powdery, white cholesterin incompletely soluble to 1 percent in absolute alcohol (99+ percent) has been found to give too sensitive results.

It is held at an angle again, and the proper amount of antigen is pipetted against the side of the neck of the bottle from a finely graduated pipette.

The bottle is promptly stoppered (preferably with a glass stopper) and shaken vigorously (the fluid thrown from bottom to cork and back) for 1 minute.

Lastly, the 0.85-percent sodium chloride solution is allowed to run in quite rapidly, the bottle is stoppered again and shaken less vigorously than previously for 1 minute.

In preparing the emulsions, the cholesterin should be pipetted with the left hand while the bottle is rotated or shaken with the right hand to insure mixture of the cholesterin solution with as much water as possible. In shaking the bottle vigorously after addition of the antigen, it is not necessary to strike the bottle against the free hand. No less vigorous shaking can be secured by striking hand against hand. Even after satisfactory shaking of the mixtures, some of the cholesterin crystals (in small clumps) will remain uncoated and in some slide tests these can be observed on the surface of the mixture. Such uncoated clumped crystals do not resemble the specific clumps of altered coated crystals and should offer no difficulty in reading the results. Emulsions may be prepared with twice, one-half, and even one-fourth of the standard formula if proper sized bottles are employed (smaller bottles for the smaller amounts).

The emulsion, when examined under the microscope at a magnification of about 120 times, shows numerous very fine particles but no clumps whatever.

FOR DIAGNOSTIC TEST

Place 1 cc. or more of the emulsion in a narrow test tube (12 mm. inside diameter) in a water bath at 35° C. (beaker of water in usual laboratory air incubator at about 37° C.) for 15 minutes. The emulsion as soon as heated is ready for use.

FOR EXCLUSION TEST

Place 2 cc. of the emulsion in a narrow test tube (12 mm. inside diameter) in a water bath at 56° C. for 15 minutes. Then pour into a 3- by 1-inch tube and centrifuge for 15 minutes (eighth setting rheostat, centrifuge size 1, type SB). Decant the fluid and, with the tube inverted, dry the inside of the tube with a cloth almost to the level of the sediment. To the sediment add 1.0 cc. of 0.85 percent sodium chloride solution.[3] Transfer to a narrow tube for use.

FOR CONTROL EXCLUSION TEST (*4*)

1. Pipette into a 1-ounce bottle 1 cc. of 1 percent standard cholesterin solution.

[3] It may require a little experimentation with time and speed of centrifugation and quantity of saline to take up the sediment (1 cc. to 1.5 cc.) to make sure that the exclusion test emulsion contains the optimal number of particles.

2. Pipetting with the left hand, allow 0.85 cc. of distilled water (pH about 6) to mix drop by drop with the cholesterol solution, rotating the bottle with the right hand during the mixture and for 10 seconds thereafter on a flat surface.

3. Add 0.1 cc. of standard antigen and after 5 seconds, holding the bottle by the neck, give it three circular throws with moderate vigor to distribute the antigen.

4. Allow the bottle to stand 2 minutes and again rotate it from the neck as previously.

5. Add 2.45 cc. physiologic saline solution and rotate the bottle from the neck as previously.

6. *Gently* pour the emulsion into a narrow test tube and place in the water bath at 56° C. for 10 minutes.

7. Transfer *gently* to 3 by 1 inch (colloidal gold) tube.

8. Centrifuge 5 minutes at the eighth rheostat setting as for the standard exclusion slide test emulsion.

9. Decant the supernatant fluid and *gently* take up the sediment in about 1.5 cc. of saline (it may require a little experimentation to determine the proper amount of saline to add to obtain the optimal number of particles in the emulsion).

Vigorous shaking and rotation in the preparation and subsequent handling of the emulsion must be avoided.

One-half the quantity may be made but 0.06 cc. antigen should be used (not 0.05 cc.) and the sediment, after centrifugation, should be taken up in 1 cc. saline (not 0.75 cc.).

The diagnostic exclusion and the control exclusion emulsions keep best in the refrigerator (8°–12° C.) and are satisfactory for use for at least 48 hours after preparation.

DIAGNOSTIC AND EXCLUSION MICROSCOPIC SLIDE PRECIPITATION TESTS FOR SYPHILIS WITH HEATED SERUM

1. Place 3 heated serum test slides, each with 12 small chambers, on a tray in a small holder.

2. Into each of the 36 rings, pipette 0.05 cc. of the heated serum to be tested (18 serums in duplicate).

3. After all the serums are pipetted, one drop of the diagnostic test antigen emulsion (about 0.008 cc.) is allowed to fall from a Wright pipette into one of the two portions of each serum. Into each of the other 18 duplicate serums a similar drop of exclusion test antigen emulsion is allowed to fall from a Wright pipette.

4. The slides in the holder are rotated on a flat surface for 4 minutes.[4]

[4] If a rotating machine is used, it should be standardized against hand rotation and set at more or less than 4 minutes as determined.

5. The results are examined at once through the microscope at a magnification of about 120 times (low power 16 mm. objective, eyepiece 12) with the light cut down as for the study of urinary sediments and reported in terms of pluses according to the degree of clumping and the size of the clumps.

Any spilling from the chamber makes the reaction therein unsatisfactory, and the serum concerned should be retested.

Results.—Occasionally there is atypical clumping with very strongly positive serums. Such irregular feathery clumping is not at all like the uniformly distributed small clumps of doubtful reactions with which they could be confused. It is advisable to dilute such serums with saline or negative serum, using one part of the serum in question and 1, 3, and 15 parts of saline or negative serum. The results with one or more of the diluted mixtures will be typical of the strongly positive reaction.

Interpretation of results.—The diagnostic slide test is especially valuable when positive (detecting the disease), the exclusion test especially valuable when negative (excluding the disease). For the selection of blood donors the exclusion slide test, not the diagnostic test, should be performed.

PREPARATION OF ANTIGEN EMULSIONS FOR DIAGNOSTIC AND EXCLUSION SLIDE TESTS OF SPINAL FLUID (*5*)

Formula.—0.85 cc. distilled water (pH about 6); 1.25 cc. of 1 percent cholesterin (Pfanstiehl C. P.) in absolute ethyl alcohol (99+ percent); 0.1 cc. antigen; 2.2 cc. of 0.85 percent sodium chloride (C. P. or reagent, Merck) solution (pH about 6); 8.8 cc. of the emulsion are made by using double the quantities given in the formula.

FOR DIAGNOSTIC TEST	FOR EXCLUSION TEST
Place 4 cc. of the emulsion in a narrow test tube (12 mm. inside diameter) in a water bath at 35° C. for 15 minutes. Then pour into a 3- by 1-inch tube. Centrifuge for 15 minutes (eighth setting rheostat, 1, S. B.). Decant the fluid and, with the tube inverted, dry the inside of the tube with a cloth almost to the level of the sediment. To the sediment add 1 cc. of 0.85 percent sodium chloride solution (pH about 6). Transfer to a narrow test tube for use.	Place 4 cc. of the emulsion in a narrow test tube (12 mm. inside diameter) in a water bath at 50° C. for 15 minutes. Then pour into a 3- by 1-inch tube. Centrifuge for 15 minutes (eighth setting rheostat, 1, S. B.).[5] Decant the fluid and, with the tube inverted, dry the inside of the tube with a cloth almost to the level of the sediment. To the sediment add 1 cc. of 0.85 percent sodium chloride solution (pH about 6). Transfer to a narrow test tube for use.

[5] In making up the exclusion test emulsion, the centrifugation should be varied until the proper speed and length of time for obtaining the optimal amount of sediment (number of particles) is established.

FOR CONTROL EXCLUSION TEST

The control exclusion test emulsion for spinal fluid differs from the standard exclusion test emulsion for spinal fluid in that it is heated at 56° C. for 15 minutes, whereas the latter is heated at 50° C. for 15 minutes.

These emulsions keep best in the refrigerator (8° to 12° C.) and are satisfactory for use for at least 48 hours after preparation.

DIAGNOSTIC AND EXCLUSION MICROSCOPIC SLIDE PRECIPITATION TESTS FOR SYPHILIS WITH SPINAL FLUID

PRELIMINARY PROCEDURES WITH SPINAL FLUIDS

Spinal fluids, turbid with exudate, blood, or bacteria, or containing injected substances including horse serum, are unsatisfactory for testing.[6] Spinal fluids with slight turbidity or few particles are centrifuged at high speed for 10 minutes, and the clear fluid is withdrawn or decanted. The pH should be 8 or more (thymol blue indicator).

Place the required number of test tubes, 6 by $\frac{5}{8}$ inches, each containing 5 cc. of Benedict's solution (1909–10), in a beaker (pyrex). Add water halfway to the top. Heat. Keep the tubes in vigorously boiling water for 5 minutes.

Place the tubes in a rack. After making certain that no copper reduction has occurred in any of the tubes, add to each tube, properly numbered, 0.5 cc. of spinal fluid. Shake each tube vigorously for 10 seconds.

Replace the tubes in the beaker. Add water halfway to the top. Heat. Keep the tubes in vigorously boiling water for 5 minutes.

Replace the tubes in the rack, inspecting each immediately after removal from the beaker for precipitate indicating presence of sugar.

Spinal fluids giving a negative reaction for sugar in the above test are unsatisfactory for testing for syphilis. These are fluids that have been acted upon by bacteria either inside or outside of the body. In the former case (bacterial meningitis) in which organisms and enzymes of the exudate have acted upon the sugar, the fluids may contain substances that give positive or unsatisfactory reactions in various tests for syphilis. Bacterial contamination subsequent to withdrawal of spinal fluids from cases of syphilis causes a steady loss both of sugar and of the specific reacting substance if the fluids are kept at room temperature.

On the other hand, if spinal fluids containing sugar when withdrawn from the body are kept at low temperature (8° to 10° C.)

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[6] A satisfactory rough estimate of the protein content may be made by noting the turbidity when 1 cc. of 95 percent alcohol is added to 0.25 cc. of spinal fluid. Fluids contaminated with serum give more than a heavy trace by this method.

they continue to give a positive reaction for sugar with the test described above for several weeks, and syphilitic spinal fluids under these conditions show no appreciable loss of specific reacting substance for at least a week.

The clear and cleared spinal fluids which give a positive reaction in the sugar test described above are then tested as follows:

DIAGNOSTIC AND EXCLUSION MICROSCOPIC SLIDE PRECIPITATION TESTS FOR SYPHILIS WTH SPINAL FLUID

Into each of 12 chambers (33 mm. in diameter) on 6 glass slides (in a holder tilted slightly by placing a small metal bar one-eighth inch thick under 1 long slide) deliver 0.05 cc. of 1 percent glacial acetic acid solution from a 0.2-cc. pipette graduated in thousandths. (It is of the utmost importance that the 1 percent acetic acid be carefully prepared since this reagent in stronger concentration will precipitate the emulsion.)

Into each chamber allow 0.25 cc. of the spinal fluid to be tested (6 spinal fluids in duplicate) to fall from a 1-cc. pipette graduated in hundredths. Hold the pipette directly above the acid and lastly touch the tip of the pipette at some dry portion of the chamber.

Rotate the slides in the holder on a flat surface with moderate vigor for 1 minute.

Into one-half of the chambers allow one drop (about 0.008 cc.) of diagnostic antigen emulsion to fall from a Wright pipette.

Into each of the duplicate spinal fluids one drop (about 0.008 cc.) of exclusion antigen emulsion is allowed to fall from a Wright pipette.

Rotate the slides in the holder on a flat surface with moderate vigor for 1 minute to distribute the antigen and then for 4 minutes move the holder gently but rapidly (about three complete movements a second) back and forth a distance of one-quarter to one-half inch.

The results are examined at once through the microscope at a magnification of about 120 times (objective 16 mm., eyepiece 12) with the light cut down as for the study of urinary sediments and recorded in terms of pluses according to the degree of clumping and the size of the clumps. (For ease in reading the results, the slide is tilted on a piece of metal one-eighth inch thick, one-half inch wide, and 4 inches long placed on the stage.)

REFERENCES

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(3) Green, G.: Paraffin rings on microscope slides. Am. J. Pub. Health, 1925, 15: 651.

(4) Kline, B. S.: Control antigen emulsions for microscopic slide precipitation tests for syphilis. Am. J. Clin. Path., 1937, 7: 490.

(5) Kline, B. S.; Rein, C. R.: The microscopic slide precipitation test for syphilis with spinal fluid. J. Lab. & Clin. Med., 1931, 16: 398.

THE KOLMER COMPLEMENT FIXATION TEST[1] FOR SYPHILIS

JOHN A. KOLMER, M. D.

Glassware and apparatus.—1. Pipettes (fig. 1).

1 cc. graduated in 0.01 cc. to tip.
5 cc. graduated in 0.10 cc.
10 cc. graduated in 0.50 cc.

An automatic pipette is highly recommended for rapid work and saving of time for pipetting saline solution, complement, antigen, and hemolysin in the conduct of the tests.

2. *Test tubes.*—Eighty-five by fifteen millimeters (inside diameter) with rounded bottoms and no lips.

3. *Cylinders.*—Glass-stoppered, graduated (50 or 100 cc. capacity) to be used for measuring amounts over 50 cc.

4. *Test tube racks.*—Galvanized wire racks carrying 12 rows of 6 tubes each (fig. 2).

5. *Water bath.*—Any easily regulated water bath is suitable, or a simple galvanized pan carrying water to a depth of 8 centimeters can be used satisfactorily at 55° or 37° C. (figs. 3 and 4).

6. *Refrigerator.*—Any refrigerator maintaining a temperature of 6° to 8° C. is satisfactory.

Method of cleaning glassware.—1. All glassware should be chemically clean and preferably sterile. To clean tubes and flasks, empty and rinse in running tap water; wash inside and outside in soapy water; rinse several times in running tap water and invert in wire baskets. Dry in the hot air oven at about 160° C.

2. Pipettes should be placed after use in a jar or cylinder of clean water with a pad of cotton in the bottom. To clean pipettes, rinse thoroughly in running tap water, place in a metal box or wire basket, and sterilize in the oven.

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[1] For a more detailed description of this test, including complement fixation tests for the identification of serums, blood stains, seminal stains, and for the detection of meat and milk adulteration, consult Kolmer's Serum Diagnosis by Complement Fixation, Lea and Febiger, Philadelphia, 1928. Antigens and hemolysin for the syphilis and other complement fixation tests may be purchased from the Research Institute of Cutaneous Medicine, 2101 Pine Street, Philadelphia.

All inquiries regarding this test should be addressed to Dr. J. A. Kolmer, Research Institute of Cutaneous Medicine, 2101 Pine Street, Philadelphia, Pa.

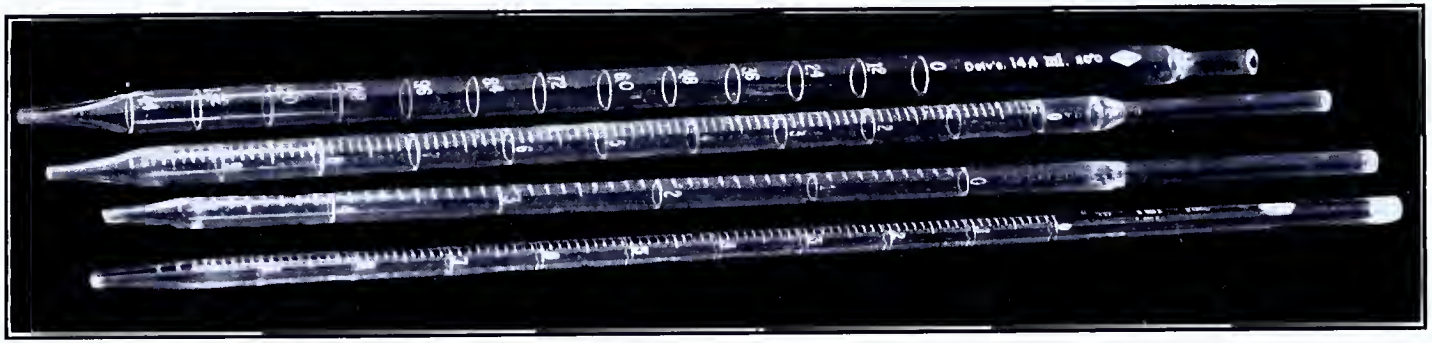

FIGURE 1.—Kolmer serologic pipettes. (From Kolmer and Boerner, Approved Laboratory Technic, 2d ed., New York, D. Appleton-Century Co. This is figure 333 on page 616.)

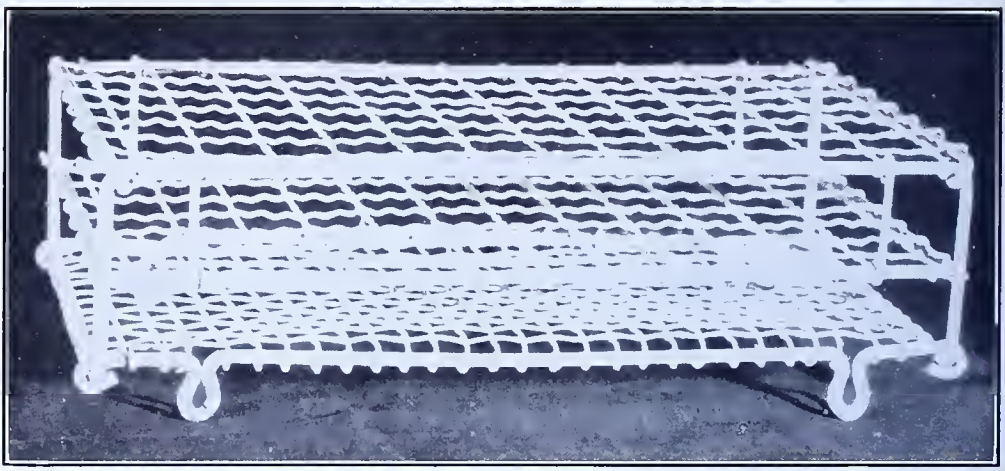

FIGURE 2.—Kolmer rack. (From Kolmer and Boerner, Approved Laboratory Technic, 2d ed., New York, D. Appleton-Century Co. This is figure 334 on page 617.)

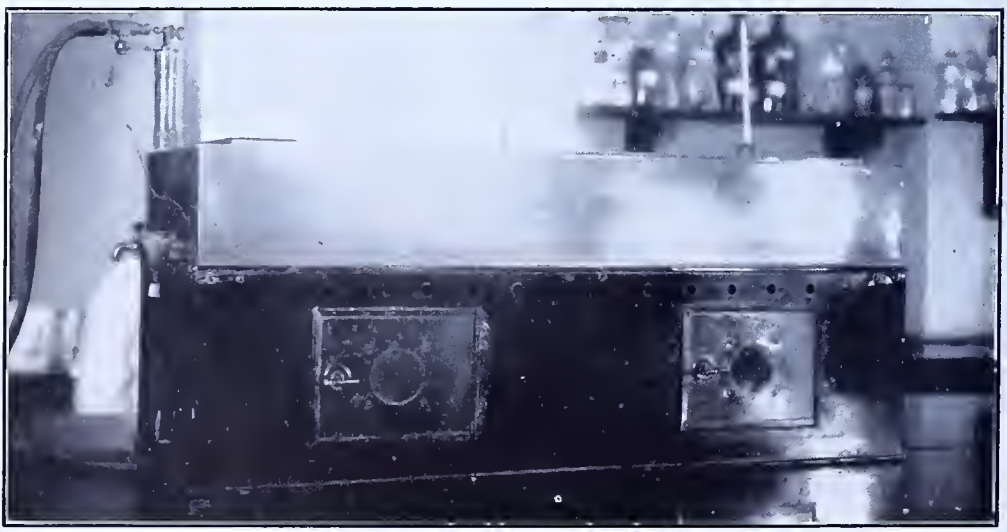

FIGURE 3.—Kolmer serologic bath, gas heated. (From Kolmer and Boerner, Approved Laboratory Technic, 2d ed., New York, D. Appleton-Century Co. This is figure 335 on page 617.)

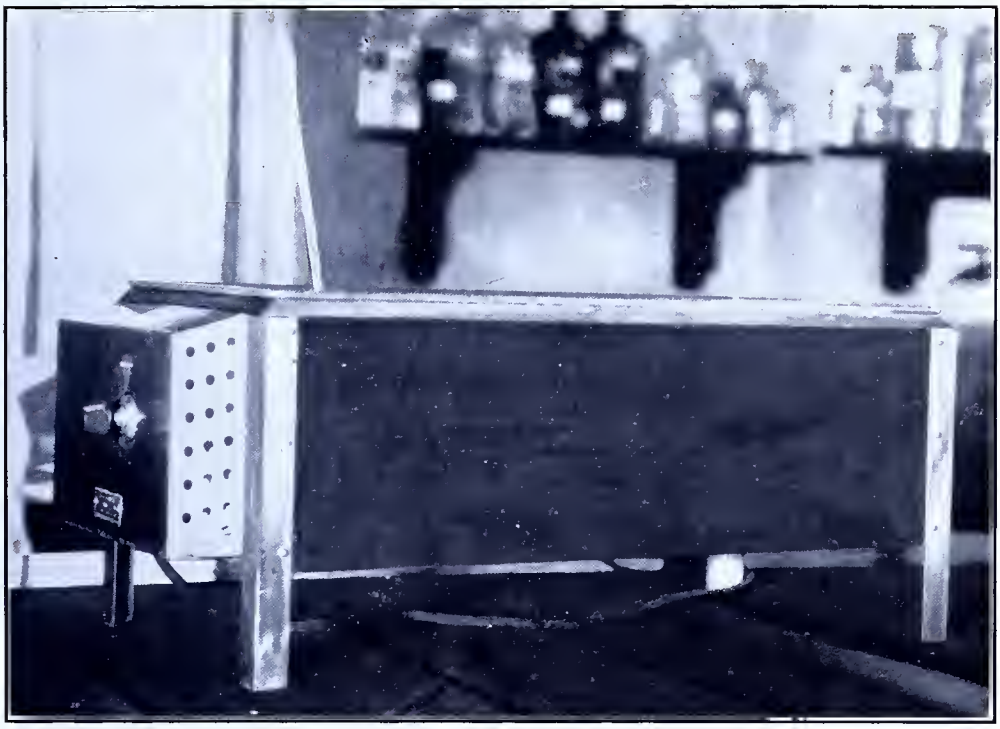

FIGURE 4.—Kolmer serologic bath, electrically heated. (From Kolmer and Boerner, Approved Laboratory Technic, 2d ed., New York, D. Appleton-Century Co. This is figure 336 on page 617.)

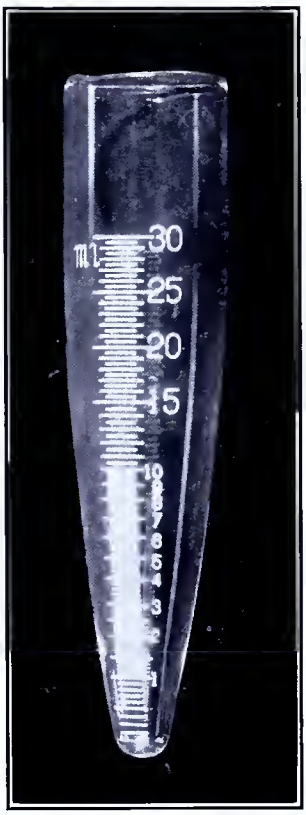

FIGURE 5.—Kolmer centrifuge tube. (From Kolmer and Boerner, Approved Laboratory Technic, 2d ed., New York, D. Appleton-Century Co. Tbis is figure 338 on page 618.)

3. Flasks should be plugged with cotton and sterilized in the oven for 30 minutes at 160° C.

4. If glassware becomes cloudy, immerse in bichromate cleaning fluid (2 parts potassium bichromate, 3 parts commercial sulfuric acid, and 25 parts water) for 24 hours. Rinse thoroughly in running tap water and proceed with the washing as described.

Preparation of saline solution.—Dissolve 8.5 gm. of dry, chemically pure sodium chloride and 0.1 gm. magnesium sulfate in 1,000 cc. of freshly distilled water. If the salt has absorbed moisture it should be dried in the hot-air oven for 10 or 15 minutes before weighing. Filter solution through paper into a flask fitted with a gauze-covered cotton stopper. Sterilize by heating in an Arnold sterilizer for 1 hour before use (not essential if immediately used).

A satisfactory saline solution should not of itself be hemolytic when 1 or 2 drops of washed corpuscles are added to 5 cc. of the solution in a test tube followed by water bath incubation for 1 hour. Neither should it be antihemolytic as determined by the hemolysin or complement titrations. The antisheep hemolysin should give a unit of at least 0.5 cc. of a 1:4,000 dilution when titrated with 0.3 cc. of 1:30 complement and 0.5 cc. of a 2 percent suspension of washed sheep corpuscles with a water bath incubation of 1 hour. It is possible that failure of hemolysis may be due to defective hemolysin or complement or to the use of corpuscles of increased resistance to serum hemolysis.

Preparation of sheep corpuscles (indicator antigen).—Sheep blood may be obtained at an abattoir or by bleeding a sheep from the external jugular vein. In a clean (but not necessarily sterile) quart-sized Mason jar, place 30 cc. of a 10-percent solution of sodium citrate in saline solution and 2 cc. of formalin. At the abbatoir have the jar almost filled with *fresh* blood (blood kept over in buckets is unsatisfactory), screw on the top, mix well with the citrate-formalin solution, and keep in a refrigerator. Ordinarly it is fit for use over a period of 2 to 3 weeks at least, but as soon as the corpuscles become too fragile a fresh supply should be secured. Boerner and Lukens advise keeping blood for 48 hours in the refrigerator before using.

If preservation is not desired, glass beads alone may be placed in the jar, and, after filling with blood, it should be thoroughly shaken for defibrination. Blood collected in this manner will keep at a low temperature (jar placed on a block of ice) for about a week. If beef blood is used, it may be collected by either method.

Filter a small quantity of blood through cotton into a *graduated* centrifuge tube (fig. 5). Allow twice as much blood as the amount of cells required. Add 2 or 3 volumes of saline solution. Centri-

fuge at a moderate velocity until it is ascertained that all the corpuscles are thrown down.

Remove the supernatant fluid with a capillary pipette or by suction. Add 3 or 4 volumes of saline solution; mix by inverting and centrifuge again for the same length of time.

Repeat the process for a third time but centrifuge twice as long as in the first washing in order to pack the cells evenly and firmly.

Cells should be washed until the supernatant fluid is almost colorless. Three washings are usually sufficient. (If more than four washings are necessary, the cells are too fragile for use.)

Read the volume of cells in the centrifuge tube, carefully remove the supernatant fluid, and prepare a 2-percent suspension by washing the corpuscles into a flask with 49 volumes of saline solution or dilute 2 cc. of corpuscles with 98 cc. of saline solution. *Always shake before using to secure an even suspension, as the corpuscles settle to the bottom of the flask when not in use.*

Preparation of antisheep hemolysin.—Give a rabbit 5 or 6 intravenous injections of 5 cc. of a 10-percent suspension of washed sheep corpuscles every 5 days. Bleed the rabbit 7 to 9 days after the last injection if a preliminary titration gives a unit of 0.5 cc. of 1:4,000 or higher. Separate the serum (it need not be inactivated) and preserve with an equal part of best grade neutral glycerin. Keep in a refrigerator.

Preparation of complement.—The pooled serums of at least 3 healthy guinea pigs should be used. Select large, well-nourished animals that have not been fed for 12 hours; avoid pregnant animals.

Anesthetize the pig lightly with ether or stun the animal with one or two sharp blows on the head. Sever the large blood vessels on both sides of the neck, being careful not to cut the esophagus or trachea. Collect the blood in a centrifuge tube by means of a large funnel. Place the blood in an incubator at 38° C. for 1 hour; break up the clot and centrifuge. Separate the clear serum. *Keep in the refrigerator when not in use.*

If but a small amount of serum is required, 4 or 5 cc. of blood may be obtained from each pig by bleeding from the heart with a 5-cc. syringe fitted with a short needle, gage 20.

Complement serum may be preserved for several weeks by adding 0.3 gm. of C. P. sodium chloride to each cc. of serum. Keep in a dark glass bottle at or near the *freezing point.* To prepare for use, dilute 1 cc. of serum with 29 cc. of distilled water. This gives a 1:30 dilution in 1-percent salt solution. Complement may also be preserved for at least 2 weeks by adding and dissolving 1 gm. of chem-

ically pure sodium acetate in each 10 cc. of serum (Rhamy). Sonnenschein's solution is also recommended:

Sodium acetate (C. P.)	12.0 gm.
Boric acid	4.0 gm.
Sterile distilled water	100.0 cc.

Equal parts of serum and solution are mixed giving a 1:2 dilution of complement from which a 1:30 dilution is prepared by diluting 1 cc. with 14 cc. of saline. By whatever of these chemical methods complement is preserved it is important to keep the serum frozen or at a temperature not exceeding 2° C. As preserved complement loses first in fixability by syphilis antigen and antibody, it should not be kept for more than 3 or 4 weeks.

Lyophil complement.—The most satisfactory method for preserving complement is by evaporation in the frozen state in vacuo by the method of Flosdorf and Mudd (J. Immunol., 1935, 29:389). It retains both hemolytic activity and fixability for 8 to 12 months and has proven satisfactory. It has the great advantage of being prepared of the pooled serums of a large number of guinea pigs with uniform hemolytic activity and fixability by antigen and antibody. It may be obtained from Sharp and Dohme, Philadelphia, and is dispensed in vacules containing the equivalent of 5 cc. of fresh serum. They should be kept in a refrigerator until used. By adding 5 cc. of distilled water the material goes into immediate solution and is ready for use in the same manner as fresh serum. Preservation by the *cryochem process* is also recommended and more economical.

Preparation of antigen.—A cholesterolized and lecithinized alcoholic extract of heart muscle is employed. Bacto beef heart, prepared by the Digestive Ferments Co. of Detroit, is recommended.

1. Place 30 gm. of beef-heart powder in a flask with 100 cc. of chemically pure acetone. Stopper tightly. Keep at room temperature for 5 days with brief shaking each day.

2. Filter through fat-free paper or decant and discard the filtrate.

3. Dry the residue and extract with 100 cc. of chemically pure absolute ethyl alcohol in a tightly stoppered flask for 5 days at room temperature, shaking each day.

4. Filter through fat-free paper with slight sqeeezing of the tissue.

5. Measure the filtrate and add absolute ethyl alcohol to 100 cc.; add 0.2 gm. of cholesterol. The cholesterol is dissolved in 10 cc. of ether and added to the alcoholic filtrate. Shake thoroughly and place in a water bath at 55° C. for 1 hour to aid solution.

6. Allow to stand at room temperature for 2 or 3 days with brief shaking each day. Filter through fat-free paper.

7. Keep the antigen at *room temperature* in a tightly stoppered bottle.

A *new antigen* of increased sensitiveness with practically no change in hemolytic or anticomplementary activity may be prepared in the same manner except that it is reinforced with acetone insoluble lipoids as follows:

(*a*) Step 1, 2, 3, and 4 as above.

(*b*) Save the first 4 ether extracts used in the preparation of Kahn or Eagle antigens. Concentrate to about one-fifth volume in an evaporating dish and add 3 to 6 volumes of acetone. After mixing and setting aside overnight, the supernatant acetone is removed and the residue of acetone-insoluble lipoids kept in a refrigerator.

(*c*) Measure the alcoholic filtrate and add absolute ethyl alcohol to 100 cc. Dissolve 0.2 gm. of cholesterol and 1 gm. of the acetone-insoluble lipoids in 20 cc. of ether and add to the alcoholic extract in a tightly stoppered bottle or flask.

(*d*) Shake thoroughly and place in a water bath at 55° C. for 1 hour to aid in the solution of the lipoids.

(*e*) Allow to stand at room temperature for 2 or 3 days with brief shaking each day. Filter through fat-free paper.

(*f*) Keep at *room temperature*. Do not disturb any sediment that may be present.

Preparation of serums.—1. All specimens are lined up and properly labeled.

2. The serums are removed from the clots with capillary pipettes to test tubes properly labeled. Great care is required to prevent errors in labeling and confusion of serums. Each serum should be free of corpuscles, otherwise it is necessary to break up the clots with wooden applicators (one for each serum) and centrifuging for clear serum. Slight tinging with hemoglobin does no harm. Serums containing large amounts of hemoglobin are likely to be anticomplementary and unsatisfactory for both complement fixation and precipitation tests.

3. It is not necessary to remove the natural antisheep hemolysins by absorption with *thoroughly washed sheep corpuscles* although this tends to increase the sensitiveness of complement fixation reactions and especially in the case of serums containing small amounts of syphilis antibody. Kolmer recommends the routine removal of natural hemolysins when conditions permit in order to secure reactions of maximum sensitiveness, but when large numbers of serums require testing it may be omitted. The method for removal of natural antisheep hemolysins from serums is as follows:

(*a*) To each is added *a drop of washed sheep corpuscle sediment for approximately each 2 cc. of blood and serum* as gaged by inspection.

(*b*) Each specimen is then thoroughly mixed with a wooden applicator (one for each serum).

(*c*) All are then placed in a *refrigerator for 15 minutes* to enable the sheep corpuscles to absorb the hemolysins with none or but a minimum and harmless amount of hemolysis.

(*d*) All specimens are now centrifuged and the serums separated into test tubes properly labeled.

4. The tubes of plain or absorbed serums are now placed in a water bath at 55° C. for *15 to 20 minutes*, when they are ready for testing.

Preparation of spinal fluids.—These are usually tested without any preliminary preparation as they do not contain enough natural anti-sheep hemolysin to require removal or enough complement to require inactivation by heating at 55° C. If a specimen contains considerable blood which has not had time to settle out, it should be centrifuged. Otherwise no preparation is required as spinal fluids are tested as delivered without preliminary heating unless they are more than 3 days old, in which case they may be heated at 55° C. for 15 minutes to remove thermolabile anticomplementary substances. As a general rule, however, spinal fluids are not anticomplementary unless heavily contaminated with bacteria (cloudy).

Titration of hemolysin.—It is advisable (but not absolutely necessary) to make this titration each time the complement fixation test is conducted.

Prepare a stock dilution of 1:100 hemolysin as follows:

	Cc.
Glycerinized hemolysin (50 percent)	2.0
Saline solution	94.0
Phenol (5 percent in saline solution)	4.0

This may be kept in the refrigerator for several weeks.

For titration, dilute to 1:1,000 (0.5 cc. of 1:100+4.5 cc. saline solution).

In a series of 10 tubes, prepare higher dilutions as follows:

No. 1.—0.5 cc. hemolysin (1:1,000)=1:1,000.
No. 2.—0.5 cc. hemolysin (1:1,000)+0.5 cc. saline solution=1:2,000.
No. 3.—0.5 cc. hemolysin (1:1,000)+1.0 cc. saline solution=1:3,000.
No. 4.—0.5 cc. hemolysin (1:1,000)+1.5 cc. saline solution=1:4,000.
No. 5.—0.5 cc. hemolysin (1:1,000)+2.0 cc. saline solution=1:5,000.
No. 6.—0.5 cc. hemolysin (1:3,000)+0.5 cc. saline solution=1:6,000.
No. 7.—0.5 cc. hemolysin (1:4,000)+0.5 cc. saline solution=1:8,000.
No. 8.—0.5 cc. hemolysin (1:5,000)+0.5 cc. saline solution=1:10,000.
No. 9.—0.5 cc. hemolysin (1:6,000)+0.5 cc. saline solution=1:12,000.
No. 10.—0.5 cc hemolysin (1:8,000)+0.5 cc. saline solution=1:16,000.

Mix the contents of each tube thoroughly.

Prepare 1:30 dilution of complement for hemolysin and complement titration by diluting 0.2 cc. of complement serum with 5.8 cc. of saline solution.

Prepare a 2-percent suspension of sheep corpuscles.

In a series of 10 tubes set up the hemolysin titration as shown in the following table:

Tube	Hemolysin, 0.5 cc.	Complement (1:30)	Saline Solution	Corpuscles
		Cc.	*Cc.*	*Cc.*
1	1:1,000	0.3	1.7	0.5
2	1:2,000	.3	1.7	.5
3	1:3,000	.3	1.7	.5
4	1:4,000	.3	1.7	.5
5	1:5,000	.3	1.7	.5
6	1:6,000	.3	1.7	.5
7	1:8,000	.3	1.7	.5
8	1:10,000	.3	1.7	.5
9	1:12,000	.3	1.7	.5
10	1:16,000	.3	1.7	.5

Mix the contents of each tube and incubate in the water bath at 38° C. for 1 hour. Read the unit of hemolysin. The *unit is the highest dilution of hemolysin that gives complete hemolysis.*

Two units are used in the complement and antigen titrations and in the complement fixation tests. Hemolysin is so diluted that 0.5 cc. contains 2 units. For example, if the unit equals 0.5 cc. of 1:6,000, two units equals 0.5 cc. of 1:3,000. Dilute just enough hemolysin for the complement titration and the complement fixation tests. *Keep hemolysin and corpuscles in suspension in the refrigerator when not in use.*

The following table shows how the dilutions are made so that 0.5 cc. carries two units:

1 unit 0.5 cc. of—	2 units would be 0.5 cc. of —	Prepared by diluting 1 cc. of stock 1:100 with following amounts of saline
		Cc.
1:1,000	1:500	4
1:2,000	1:1,000	9
1:3,000	1:1,500	14
1:4,000	1:2,000	19
1:5,000	1:2,500	24
1:6,000	1:3,000	29
1:8,000	1:4,000	39
1:10,000	1:5,000	49

High titer hemolysin is recommended and the unit should be 0.5 cc. of 1:4,000 or higher.

In practice the hemolysin titration may be placed in the water bath at the same time as the complement titration; at the end of the first incubation of the complement titration the unit of hemolysin is available and two units are added to all tubes of the complement titration, etc.

Complement titration.—For the complement titration use 1:30 dilution of complement prepared above. *Dilute antigen so that the dose employed in the main tests is contained in 0.5 cc.* This dilution is made by placing the required amount of saline solution in a flask and adding antigen drop by drop. Shake the flask after each addition of antigen. Prepare enough antigen dilution for the complement titration and the complement fixation tests.

In a series of 10 test tubes set up, the complement titration is as follows:

Tube	Complement, cc. (1:30)	Antigen dose, cc.	Saline solution, cc.	Water bath 37° C. for 1 hour	Hemolysin, cc. (2 units)	Corpuscles, cc. (2 percent)	Water bath 37° C. for 1 hour
1	0.1	0.5	1.4		0.5	0.5	
2	.15	.5	1.4		.5	.5	
3	.2	.5	1.3		.5	.5	
4	.25	.5	1.3		.5	.5	
5	.3	.5	1.2		.5	.5	
6	.35	.5	1.2		.5	.5	
7	.4	.5	1.1		.5	.5	
8	.45	.5	1.1		.5	.5	
9	.5	.5	1.0		.5	.5	
10	None	None	2.5		None	.5	

The smallest amount of complement just giving complete sparkling hemolysis is the *exact unit.* The next higher tube is the *full unit* which contains 0.05 cc. more complement. In conducting the antigen titration and complement fixation tests, *two full units* are employed and so diluted as to be contained in 1 cc. as per the following example:

Exact unit: 0.3 cc.
Full unit: 0.35 cc.
Dose (two full units): 0.7 cc.

To calculate the dilution to employ so that 1 cc. contains the dose of two full units, divide 30 by the dose: $\frac{30}{0.7}=43$ or 1 cc. of 1:43 dilution of serum.

The following table gives additional examples:

Exact unit, cc.	Full unit, cc.	Two full units, cc.	Dilution to use	Preparation
0.2	0.25	0.5	1:60	1 cc. serum+59 cc. saline.
.25	.3	.6	1:50	1 cc. serum+49 cc. saline.
.3	.35	.7	1:43	1 cc. serum+42 cc. saline.
.35	.4	.8	1:37	1 cc. serum+36 cc. saline.
.4	.45	.9	1:33	1 cc. serum+32 cc. saline.
.45	.5	1.0	1:30	1 cc. serum+29 cc. saline.
.5	.55	1.1	1:27	1 cc. serum+26 cc. saline.

If, however, the complement is unusually sensitive to the anti-complementary effects of antigen and serum in the conduct of the complement fixation tests, as is sometimes the case during the hot

summer months, 2½ exact units may be employed and so diluted that 1 cc. contains this dose. Example:

Exact unit: 0.35 cc.
2½ units: 0.88 cc.

To calculate the dilution to use so that 1 cc. contains the dose, divide 30 by the dose: $\frac{30}{0.88}=34$ or 1 cc. of 1:34 dilution of serum.

The following table gives additional examples:

Unit cc.	2½ units, cc.	Dilution to use	Preparation
0.2	.50	1:60	1 cc. serum+59 cc. saline.
.25	.63	1:47	1 cc. serum+46 cc. saline.
.3	.75	1:40	1 cc. serum+39 cc. saline.
.35	.88	1:34	1 cc. serum+33 cc. saline.
.4	1.0	1:30	1 cc. serum+29 cc. saline.
.45	1.13	1:27	1 cc. serum+26 cc. saline.
.5	1.25	1:24	1 cc. serum+23 cc. saline.

It is always advisable to dilute complement serum with cold saline solution instead of with saline kept at room temperature. Undiluted and especially diluted complement serum should always be kept in a refrigerator when not in use. Exposure of diluted complement to room temperature for over an hour may result in some deterioration.

Occasionally hyperactive complement yields a unit of 0.1 to 0.25 cc. of 1:30, but when this occurs it is necessary to take arbitrarily 0.3 cc. as the exact unit as less complement falls below the absolute minimum and is likely to be unsatisfactory.

Titration of antigen.—It is not necessary to titrate for hemolytic and anticomplementary units as hitherto advised because titrations of over 280 antigens by Kolmer during the past 14 years have never shown any to be hemolytic in 0.5 cc. of 1:4 and the anticomplementary units have been uniformly from 0.5 cc. of 1:6 to not higher than 1:10. Therefore, these titrations may be omitted, providing the antigen is prepared by either of the methods described. It is, however, necessary to titrate for *antigenic activity* and the following method of Boerner and Lukens is recommended:

1. Prepare a 1:8 dilution of antigen by adding 0.1 cc., drop by drop with shaking between each, to 7.9 cc. of saline solution in a large test tube or small flask. Higher dilutions are then prepared as follows:

4 cc. of 1:80+4 cc. saline solution=1:160.
4 cc. of 1:160+4 cc. saline solution=1:320.
4 cc. of 1:320+4 cc. saline solution=1:640.
4 cc. of 1:640+4 cc. saline solution=1:1280.
4 cc. of 1:1280+4 cc. saline solution=1:2560.

2. Arrange five rows of test tubes with six in each row. In the *first* tube of each row place 0.5 cc. of antigen 1:80; in the *second* tube of each row 0.5 cc. of antigen 1:160; in the *third* tube, 0.5 cc. of 1:320; in the *fourth*, 0.5 cc. of 1:640; in the *fifth* 0.5 cc. of 1:1280; and in the *sixth* 0.5 cc. of 1:2560.

3. Heat 3 cc. of a moderately to strongly positive syphilitic serum in a water bath at 55° C. for 15 to 20 minutes and prepare 5 dilutions as follows in large test tubes:

1.0 cc. serum+4.0 cc. saline=1:5 (0.5 cc. carries 0.1 cc. serum).
0.5 cc. serum+4.5 cc. saline=1:10 (0.5 cc. carries 0.05 cc. serum).
0.5 cc. serum+9.5 cc. saline=1:20 (0.5 cc. carries 0.025 cc. serum).
2.0 cc. serum 1:20+2.0 cc. saline=1:40 (0.5 cc. carries 0.0125 cc. serum).
1.0 cc. serum 1:20+4.0 cc. saline=1:100 (0.5 cc. carries 0.005 cc. serum).

4. Add 0.5 cc. of 1:5 dilution to each of the six tubes of the first row; 0.5 cc. of 1:10 to each tube of the second row; 0.5 cc. of 1:20 to each tube of the third row; 0.5 cc. of 1:40 to each tube of the fourth row; and 0.5 cc. of 1:100 to each tube of the fifth row.

5. Add 1 cc. of complement dilution carrying 2 full units to all tubes.

6. Put up a *serum control* carrying 0.5 cc. of 1:5 serum and 1 cc. of complement (2 full units); also a *hemolytic system control* carrying 1 cc. of saline solution and 1 cc. of complement (2 full units).

7. Shake the tubes gently and place in refrigerator at 6° to 8° C. for 15 to 18 hours, followed by water bath at 37° C. for 10 minutes.

8. Add 0.5 cc. of hemolysin (2 units) and 0.5 cc. of 2 percent suspension of corpuscles to all tubes.

9. Mix thoroughly and place in a water bath at 37° C. for 1 hour; make readings. The serum and hemolytic system controls should show complete hemolysis.

10. Chart the results as per the following example observed with a strongly positive serum:

Serum in 0.5 cc.	Antigen in 0.5 cc. amounts					
	1:80	1:160	1:320	1:640	1:1280	1:2560
0.005	−	−	++	−	−	−
0.0125	−	+	++++	++++	++	+
0.025	+	++++	++++	++++	++++	+
0.05	+++	++++	++++	++++	++++	++
0.1	++++	++++	++++	++++	++++	+++

11. The dose of antigen to employ in the main tests is the *largest amount giving a + + + + reaction with the smallest amount of serum.* If three dilutions of antigen give + + + + reactions with the smallest amount of serum, the dose to use should be midway between the highest and lowest.

Choice of complement fixation methods.—Two methods are available. One, the *quantitative test*, employs five doses of serum or spinal fluid and is generally preferred, especially in testing the serums of cases of syphilis under treatment in order to secure serologic evidences of improvement. The second, designated as the *simplified test*, uses one dose of serum (0.2 cc.) with an additional second tube as a control (0.2 cc.) and is sufficient for diagnostic purposes as well as being more economical of materials and time required. It possesses the same specificity as the quantitative test but is not quite as sensitive. The test may be conducted also with a single dose of 0.1 cc. of serum with 0.1 cc. in the serum control although the reactions are not quite as sensitive as tests employing 0.2 cc. of serum.

The quantitative complement fixation test.—1. *For each serum.*—(*a*) Arrange six test tubes and place in them the following amounts of saline solution respectively: 0.9, 0.5, 0.5, 0.5, 2.0 and 0.5 cc.

(*b*) To tube No. 1 add 0.6 cc. of inactivated serum. Mix by drawing up in the pipette several times and transfer 0.5 cc. to No. 2 and 0.5 cc. to No. 6 (serum control).

(*c*) Mix No. 2 and transfer 0.5 cc. to No. 3.

(*d*) Mix No. 3 and transfer 0.5 cc. to No. 4.

(*e*) Mix No. 4 and transfer 0.5 cc. to No. 5; mix and discard 2.0 cc.

This leaves 0.5 cc. in each of the first 5 tubes carrying the following amounts of serum 0.2, 0.1, 0.05, 0.025, and 0.005 cc.; No. 6 (the serum control) carries 1.0 cc. or 0.2 cc. of serum since it receives no antigen, thereby making the total volume in all tubes the same when the test is finished.

2. *For each spinal fluid.*—(*a*) Arrange six tubes and place 0.5 cc. saline solution in tubes 2, 3, 4, 5, and 6.

(*b*) In tubes 1, 2, and 6 place 0.5 cc. spinal fluid. Mix No. 2 and transfer 0.5 cc. to No. 3. Mix No. 3 and transfer 0.5 cc. to No. 4. Mix No. 4 and transfer 0.5 cc. to No. 5. Mix No. 5 and discard 0.5 cc.

(*c*) Tubes 1 to 5 now contain 0.5 cc. carrying 0.5, 0.25, 0.125, 0.0625, and 0.03125 cc. of spinal fluid. Tube 6 (control) contains 1 cc. carrying 0.5 cc. of spinal fluid.

3. To the first five tubes of each set of serum or spinal fluid add 0.5 cc. of diluted antigen carrying the proper dose.

4. After an interval of 10 to 30 minutes, add 1 cc. complement (2 full units) to each tube.

5. Include the following controls:

Antigen control containing 0.5 cc. diluted antigen, 0.5 cc. saline solution, and 1.0 cc. diluted complement (2 full units).

Hemolytic system control containing 1 cc. saline solution and 1 cc. diluted complement.

Corpuscle control containing 2.5 cc. salt solution.

Positive and negative serum controls should be included.

6. Mix the contents of each tube by gently shaking and place in the refrigerator at 6° to 8° C. for 15 to 18 hours.

7. Place tubes in the water bath at 37° C. for 10 to 15 minutes (not longer).

8. To all tubes, except the corpuscle control, add 0.5 cc. of hemolysin (carrying 2 units) and to all tubes add 0.5 cc. of 2 percent corpuscle suspension (shaken up).

9. Mix the contents of each tube by gently shaking and place in the water bath at 37° C. for 1 hour when the readings are made. *More sensitive readings may be made 10 minutes after the antigen, hemolytic system, and serum controls show complete hemolysis and are preferred.*

10. The following table shows the set-up for the quantitative complement fixation test with serum:

Tube	Patient's serum in 0.5 cc.	Antigen cc.	Interval of 10 to 30 minutes at room temperature	Complement cc. (2 full units)	Primary incubation in refrigerator at 6° to 8° C. for 15 to 18 hours followed by 10 to 15 minutes at 37° C.	Hemolysin cc. (2 units)	Corpuscles cc. (2 percent)	Secondary incubation in water at 37° C.
1	0.2 cc	0.5		1.0		0.5		
2	0.1 cc	.5		1.0		.5	0.5	
3	0.05 cc	.5		1.0		.5	.5	
4	0.025 cc	.5		1.0		.5	.5	
5	0.005 cc	.5		1.0		.5	.5	
6	0.2 cc (control)	None		1.0		.5	.5	
7	Antigen control: 0.5 cc. saline solution	.5		1.0		.5	.5	
8	Hemolytic control: 1.0 cc. saline solution	None		1.0		.5	.5	
9	Corpuscle control: 2.5 cc. saline solution	None		None		None	.5	

11. After the secondary incubation the readings may be made at once or after the tubes have been placed in the refrigerator for several hours to permit the settling of nonhemolyzed corpuscles. Read the degree of inhibition of hemolysis and record for each tube as: − (complete hemolysis); + (25 percent inhibition recorded as 1); ++ (50 percent inhibition recorded as 2); +++ (75 percent inhibition recorded as 3); ++++ (100 percent inhibition recorded as 4). All serum, antigen, and hemolytic controls should show complete hemolysis. The corpuscle control should show no hemolysis.

12. Reactions may be interpreted as follows:

(*a*) *Very strongly positive* when *complete fixation* (++++) occurs in the third and fourth or fifth tubes. Examples: 44444; 4444−; 4442−; 444−−; 344−−.

(*b*) *Strongly positive* when *complete fixation* (++++) occurs in the second tube.

Examples: 4431−; 442−−; 342−−; 44−−−.

(*c*) *Moderately positive* when *complete fixation* (++++) occurs in the first tube.

Example: 431−−; 42−−−; 4−−−−.

(*d*) *Weakly positive* when *partial fixation* occurs in one or more tubes.

Examples: 321−−; 21−−−; 1−−−−.

(*e*) *Doubtfully positive* when the reaction is ± in the first tube.

Example: ±−−−−.

(*f*) *Negative* when there is complete hemolysis in all tubes.

Example: −−−−−.

The method of recording and reporting a complement fixation test by this method is according to the following examples:

Quantitative reaction	=strongly positive (442−−)
Serum 0.2 cc.	=++++
Serum 0.1 cc.	=++++
Serum 0.05 cc.	=++
Serum 0.025 cc.	=−
Serum 0.005 cc.	=−
Serum 0.2 cc. (control)	=−
Quantitative reaction	=strongly positive (42−−−)
Spinal fluid 0.5 cc.	=++++
Spinal fluid 0.25 cc.	=++
Spinal fluid 0.125 cc.	=−
Spinal fluid 0.0625 cc.	=−
Spinal fluid 0.03125 cc.	=−
Spinal fluid 0.5 (control)	=−

The American Committee on Evaluation of Serodiagnostic Tests for Syphilis has recommended reporting reactions only as positive, doubtful, or negative.

The simplified complement fixation test.—1. This test is conducted in exactly the same manner as described for the quantitative test except that one dose of *serum* (0.2 cc. with 0.2 cc. in the serum control) is employed. With *spinal fluid* a single dose of 0.5 cc. with 0.5 cc. in the control is employed. In other words the technic is exactly the same insofar as the preparation and titration of hemolysin, complement, and antigen are concerned as likewise the inclusion of anti-

gen, hemolytic system, and corpuscle controls. When large numbers of tests are conducted, controls with known positive and negative serums are not required; but otherwise, and especially in the case of inexperienced serologists, they should be included.

2. Preliminary removal of natural antisheep hemolysin is omitted.

3. Heat the serums in a water bath at 55° to 56° C. for 30 minutes. In the quantitative test, heating is for 15 to 20 minutes only and is preferred in order to reduce to a minimum the destruction of antibody, but 30 minutes may be employed so that the serums are prepared in the single operation for the Eagle, Hinton, Kahn, or Kline flocculation tests. Spinal fluids do not require heating unless kept for more than 3 days at room temperature (as during shipment in the mails) when heating at 55° to 56° C. is advisable for the removal of thermolabile anticomplementary substances.

4. For each serum arrange two test tubes and place 0.5 cc. of saline solution in the second or serum control tube.

5. For each spinal fluid arrange two test tubes; no saline solution.

6. Place 0.2 cc. of serum or 0.5 cc. of spinal fluid in each of the two test tubes.

7. Add 0.5 cc. of antigen, carrying the optimum dilution, in the first tube of each set.

8. Wait 10 minutes at room temperature when 1 cc. of complement (carrying two full units) is added to all tubes.

9. Primary incubation in a refrigerator at 6° to 8° C. for 15 to 18 hours followed by 10 to 15 minutes in a water bath at 37° C.

10. Add 0.5 cc. of hemolysin (carrying two units) and 0.5 cc. of 2-percent suspension of washed sheep corpuscles to all tubes.

11. Secondary incubation in a water bath at 37° C. for 1 hour when readings are made, although experienced serologists are advised to remove the racks and make readings 10 minutes after complete hemolysis of the serum antigen, and hemolytic system controls.

The reactions may be reported as positive, doubtful, or negative, as recommended by the Committee on the Evaluation of Serodiagnostic Tests for Syphilis of the United States Public Health Service cooperating with the American Society of Clinical Pathologists, as follows: *Positive:* ++++ (4), +++ (3), ++ (2) or + (1), in the first tube. *Doubtful:* ± in the first tube. *Negative:* − in the first tube. However, Kolmer recommends reporting as strongly positive, weakly positive, doubtful, and negative as follows: *Strongly positive:* ++++ (4) or +++ (3) in the first tube. *Weakly positive:* ++ (2) or + (1) in the first tube. *Doubtful:* ± in the first tube. *Negative:* − in the first tube.

Slightly *anticomplementary reactions* may be safely reported as follows: 4 ±=positive, 4 1=positive, 4 2=doubtful, 3 1=

doubtful, 3 ±=doubtful, 3 3=negative, 2 2=negative, 2 1=negative, 1 1=negative, 1 ±=negative, ± ±=negative.

With serums heavily contaminated with bacteria and those which are chylous or heavily tinged with hemoglobin from spontaneous hemolysis in which the presence of thermostabile anticomplementary substances is suspected, a modified Sachs method is recommended for their preparation as described later.

Modified technic for small amounts of serum and spinal fluid.—It sometimes occurs that a sufficient amount of serum or spinal fluid is not available for conducting the quantitative test. In such cases the test can be conducted in exactly the same manner as described *using all reagents in one-half the usual amounts.* The hemolysin and complement are not titrated separately for this test as the same dilutions are employed in one-half amounts. The same antigen dilution is also used but in one-half amount.

Analysis of difficulties—Defective complement.—In the great majority of instances difficulties are due to complement supersensitive to the anticomplementary effects of antigen, serum, or both. This is especially likely to occur during the hot months of the year. Sometimes complement may be defective in hemolytic activity and whenever the unit is higher than 0.5 cc. of 1:30 dilution it should not be used. But sometimes the complement is satisfactory from this standpoint but yet defective in the tests because supersensitive to antigen and prone to give prezone reactions. With negative or normal serums the reactions are apt to be −12−− or −1244 with perfect serum controls. When 2½ units of complement are used instead of 2 full units as routinely employed, this difficulty may be greatly reduced. Furthermore, under these conditions lyophil or cryochem complement is recommended since the complement is a mixture of the serums of a large number of guinea pigs and may be prepared during the colder months of the year. When fresh serum is used it is important to prepare it from several *full grown*, *healthy*, and *previously* unused pigs. As a general rule the trouble is first thought to be due to defective hemolysin but, since this reagent keeps very well, it is seldom responsible.

Defective hemolysin.—This is probably least likely to be a cause of trouble although usually first suspected, especially if the hemolysin has been previously used with success. The unit of antisheep hemolysin should be at least 0.5 cc. of 1:4,000 and serum of this and higher strengths are so easy to prepare that it is a mistake to use weaker products. If the saline solution and complement are satisfactory, a good hemolysin is rarely responsible even when shipped over long distances.

Defective corpuscles.—When blood is obtained from an abattoir one is almost sure sooner or later to encounter the corpuscles of occasional

animals possessing *increased resistance* to serum hemolysis. The cause of this phenomenon is unknown; fortunately it is rare. The remedy is to discard the corpuscles and secure a fresh supply of blood.

Anticomplementary antigen.—Providing no mistakes have occurred in dilution and dosage, this is very rarely a cause of trouble. When the antigen control shows incomplete hemolysis it is almost surely due to some component of the hemolytic system, especially the complement.

Anticomplementary serums.—Serums and spinal fluids may be found to be anticomplementary, as shown by incomplete hemolysis of the serum controls. After experience has been gained some of these reactions may be safely read, but as a general rule it is safer and wiser to repeat the tests with fresh serum, especially in the case of those technicians lacking experience in complement fixation work. It is infinitely better to repeat the tests than to run the slightest chances of error, especially the regrettable and almost unpardonable error of rendering a falsely positive report. Sometimes the majority of serums of a day's work show incomplete hemolysis of the serum controls, but this trouble is not due to anticomplementary effects on their part but rather to the use of a defective supersensitive complement. Under these conditions the tests must be repeated and for this reason the *unused portions of all serums should be routinely kept in a refrigerator until the tests are completed in case repetitions are required.*

Modified Sachs method for the quantitative test with anticomplementary serums.—Sachs has described a very useful method for testing anticomplementary serums. Serums very deeply tinged with hemoglobin do not respond quite as well to this method. Rabbit and dog serums and the serums of other of the lower animals may be treated in the same manner since it likewise removes the anticomplementary substances from the majority but not the substances responsible for the nonspecific complementary fixation reactions sometimes yielded by the normal serums of rabbits, dogs, and mules. The method has not been applied to spinal fluids.

1. Heat 0.5 cc. of serum at 55° C. for 15 minutes.
2. Add 4.1 cc. of accurately titrated N/300 hydrochloric acid and mix.
3. After standing ½ hour at room temperature, centrifuge thoroughly and discard the sediment.
4. To the supernatant fluid add 0.4 cc. of 10 percent sodium chloride solution. The acid is fixed by the precipitate of globulin; hence neutralization is unnecessary.
5. This gives a 1:10 dilution of original serum ready for testing.
6. Arrange two rows of 5 test tubes (the rear row are serum controls and receive no antigen).

7. Place 1 cc. of normal saline solution in tubes 3 and 4 and 2 cc. in tube 5 of the first row; place 0.5 cc. in each of the 5 tubes of the second row.

8. Place 1 cc. of serum diluted 1:10 in the first and third tubes of the first row and 0.5 cc. in the second tube. Mix No. 3 and transfer 1 cc. to No. 4 and 0.5 cc. to No. 3 of the second row. Mix No. 4; transfer 0.5 cc. to No. 5, 0.5 cc. to No. 4 of second row and discard 0.5 cc. Mix No. 5, transfer 0.5 cc. to No. 5 of the rear row and discard 1.5 cc.

9. Place 1 cc. of serum diluted 1:10 in No. 1 and 0.5 cc. in No. 2 of the second row.

10. Add antigen (0.5 cc. of proper dilution as used in the regular test) to each tube of the front row. Allow to stand at room temperature for 10 to 30 minutes when two full units of complement are added to all tubes of both rows and the balance of the test completed in the usual manner.

11. The tubes of the front and rear rows carry 0.1, 0.05, 0.025, 0.0125, and 0.0025 cc. of serum, respectively.

12. Upon completion of the test all of the tubes of the second row should show complete hemolysis. However, the first tube carrying 0.1 cc. and sometimes the second carrying 0.05 cc. of serum, may not show complete hemolysis. With negative serums the corresponding front tubes show the same degree of inhibition of hemolysis, and under these conditions a negative report may be rendered. With positive serums inhibition of hemolysis is much more marked in the tubes of the front row. It is advisable to report the reactions as positive, doubtful, or negative.

Modified Sachs method for the simplified test with anticomplementary serums.—1. Heat 0.5 cc. of serum at 55° to 56° C. in a water bath for 30 minutes.

2. Add 4.1 cc. of accurately titrated N/300 hydrochloric acid and mix.

3. After standing one-half hour at room temperature, centrifuge thoroughly and discard the sediment.

4. To the supernatant fluid add 0.4 cc. of 10 percent sodium chloride solution. The acid is fixed by the precipitate of globulin, hence neutralization is unnecessary.

5. This gives a 1:10 dilution of original serum ready for testing.

6. Place 1 cc. in each of two tubes and proceed as above described. In these tests the dose of diluted serum is equivalent to 0.1 instead of 0.2 cc. of undiluted serum. The reactions, however, are recorded and reported exactly as above described.

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RESOLUTIONS ADOPTED AT THE CONFERENCE ON THE CONTROL OF VENEREAL DISEASES IN THE SOUTHERN STATES

ATLANTA, GEORGIA

February 13–14, 1940

Supplement No. 12
to Venereal Disease Information

FEDERAL SECURITY AGENCY

UNITED STATES PUBLIC HEALTH SERVICE

Thomas Parran, *Surgeon General*

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FOREWORD

Under the auspices of the United States Public Health Service regional conference on venereal disease control in the Southern tates was held at the Henry Grady Hotel in Atlanta, Ga., on ebruary 13–14, 1940.

The purpose of this meeting was to afford representatives of State ealth departments and local health officers an opportunity to discuss ankly on common ground the various problems arising in connec- on with the control of syphilis and gonorrhea in the South. No rmal papers were presented. In order to bring to mind topics pon which discussion of experiences might prove of value to the roup, a tentative agenda was prepared and submitted in advance) each State health department.

Sixteen Southern States and the District of Columbia were repre- nted. The list of 133 registrants included Surg. Gen. Thomas arran, other officers of the United States Public Health Service, offi- rs of the United States Army, and State and local health officials.

The general topics considered were: Record forms, diagnostic meas- res, control through treatment, case-finding and case-holding, in- rmative program among physicians, public educational measures, dministrative problems, and qualifications of personnel. The fol- wing resolutions were evolved from the discussions and delibera- ons during the meeting and represent the crystallized opinion of ose in attendance. The resolutions as adopted are published for uture guidance.

RECORD FORMS

MINIMAL DATA TO BE INCLUDED ON THE MORBIDITY REPORT FORM

Whereas it is recognized that an effective program for the control of the venereal diseases rests in large part on the uniformity, accuracy, and completeness of reporting: Therefore be it

Resolved, That morbidity report forms adopted in the future by State departments of health should contain as a minimum the following items:

Date of report.

Name or initials of patient.

Address of patient.

Age or birth date, color, and sex of patient.

Duration of infection.

A check list for diagnosis.

Syphilis—

Acquired: Primary. Secondary.

Early latent (less than 4 years' duration).

Late latent (4 or more years' duration).

Congenital (specify manifestations).

Gonorrhea—

Genital. Eye. Other.

Chancroid.

Granuloma inguinale.

Lymphogranuloma venereum.

Laboratory confirmation of diagnosis: Dark field, blood, smear, culture, Frei, intracutaneous test for chancroid; in terms of positive, negative, doubtful, and not done.

Information concerning previous treatment, including amount of previous treatment.

Statement as to whether or not patient with syphilis is pregnant at time of beginning treatment. If pregnant, months pregnancy has advanced, or the expected date of confinement.

In those areas where facilities exist to provide the treatment source with case-holding and case-finding service, stubs should be included on the morbidity form for requesting this service. Items on such a stub might be:

Discontinued Treatment Notice.
Patient identification.
Name, address, age, color, sex.
Disease: Date of infection.
Amount of treatment before lapse.
Date of last treatment.
Date and result of last laboratory report.
With a note: The above patient has not returned for treatment since _____. I wish health department follow-up.
Identification of treatment source _____.
Section on the morbidity report form for epidemiology providing space for—
Names, address, relationship, age of all contacts within preceding 60 days and all subsequent exposures.

MINIMAL DATA FOR THE LABORATORY REPORT FORM

Whereas little uniformity exists in the informational and statistical content of laboratory reports for syphilis: Therefore be it

Resolved, That report forms adopted by the several States herein represented contain as a minimum the following items:

1. Identification of patient.
   Full name or initials.
   Address if name given, street only if not.
   Age or birth date, sex, color, marital status.
   Clinic No. and patient No. if from a clinic.
   Previous treatment.
2. Identification of physician.
   Name, address.
3. Specimen for—
   Blood serologic test.
   Dark-field examination.
   Spinal fluid examination.
   Date collected.
   Purpose for which specimen was taken.
   (*a*) Diagnostic—first test.
   (*b*) Repeat diagnostic.
   (*c*) Treatment control.
   (*d*) Premarital.
   (*e*) Pregnancy.

4. Reaction of specimen.
   Laboratory number of specimen.
   Date reported.
   Space to record results; and be it further

Resolved, That each health department receiving Federal or State aid for laboratory services should maintain a record system whereby the results of tests by color, age, and sex of patient, and by reason for running the test may easily be determined.

MINIMAL DATA FOR A SATISFACTORY HISTORY AND PHYSICAL EXAMINATION FORM

Whereas the recording of all positive and significant negative historical and physical findings, as well as the complete recording of epidemiologic, laboratory, and treatment activity on patient record forms, is fundamental to the treatment control of syphilis: Therefore be it

Resolved, That a form be adopted by every clinic treating syphilis that includes as a minimum the following items:

I. Identification of patient—
   Record number. Name (last, first, middle). Address. Age. Color. Sex. Marital status.
   Admission diagnosis. Subsequent diagnoses of progressions.

II. History and physical examination—
   Date of examination. History of previous treatment giving number of doses with first and last dates of treatment. Pregnancy history: Reason for clinic attendance and referring person or agency. Syphilitic history: Dates and character of early lesions, types and duration of late manifestations, and details of serologic history. Physical examination to include: General description of patient, examination of skin, mucous membranes, genitalia, eye, heart, lungs, lymphatic system, and common reflexes. Provisions to be made for periodic reexamination.

III. Diagnosis—
   A. Basis for: Dark-field examinations, blood serology, and spinal fluid examinations; pertinent clinical findings.
   B. Terminology, expressed as:
      1. EARLY SYPHILIS.
         a. Primary.
            1. Seronegative.
            2. Seropositive.

b. Secondary.
1. Early secondary.
2. Recurrent secondary.

2. LATENT SYPHILIS (asymptomatic)
a. Early latent (less than 4 years).[1]
b. Late latent (4 or more years).[1]

3. LATE SYPHILIS.
a. Cardiovascular.
1. Uncomplicated—aortitis.
2. Aortic regurgitation.
3. Aneurysm.
4. Other or undetermined.

b. Neurosyphilis.
1. Asymptomatic (abnormal spinal fluid, no detectable clinical signs or symptoms).
2. Tabes dorsalis.
3. Paresis.
4. Taboparesis.
5. Other or undetermined.

c. Other than cardiovascular or central nervous system syphilis.
1. Skin.
2. Bone.
3. Liver.
4. Other visceral.

4. CONGENITAL SYPHILIS.
a. Early (less than 3 years of age).
b. Late (over 3 years of age).
1. Skin and mucous membrane.
2. Bone and joint.
3. Interstitial keratitis.
4. Central nervous system (state type).
5. Other.

IV. Social and Epidemiologic—
A. Household roster.
B. Contacts—Age, color, sex, address, with provisions to note investigation, examination results, and history number if under treatment.
C. Case-holding efforts: Interviews, home visits, correspondence, etc.

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[1] Following the suggestion that an arbitrary age should be set as the dividing line between "early latent" and "late latent," the chair ruled that when the exact date of infection is not determinable, each clinic will be expected to set some arbitrary age or date limit.

V. Special Examinations—
   A. Eye.
   B. Heart.
   C. Neurologic and psychiatric.
   D. Hematology.
   E. Kidney function.

VI. Treatment record to provide space for the entry of date, number of the dose, type of drug, dose of drug, and provision for frequent or automatic summarization of treatment.

Reaction to therapy. Laboratory note—Periodic blood and spinal fluid findings. Clinical progress notes which should include frequent clinical evaluation of the results of treatment; and be it further

Resolved, That all of the above-enumerated items be incorporated in he patient's individual record form.

MINIMAL DATA TO BE INCLUDED ON THE EPIDEMIOLOGIC REPORT

Whereas there are a variety of State and local forms now employed for the procuring and recording of epidemiologic data; and

Whereas there is frequent need for the exchange of comparable nformation on this subject: Therefore be it

Resolved, That epidemiologic records provided in the future by he State departments of health contain the following minimal data:

I. Contact Record Slip—
   Name of treatment source _____ Date _____.
   Name or description of contact, age, sex, color, marital status.
   Address or information leading to location of contact.
   Clinic number of informant.
   Date of contact.
   Indication of urgency: Grade I, II, III (determined by stage of infection in original case).
   Date or dates of visit to contact, results of visits.
   Cooperative—given clinic appointment.
   Cooperative—will consult private physician.
   Moved—unable to locate.
   Moved—give new address.
   Interviewed but uncooperative (refer to Health Officer).

II. Lapsed Patient Record—
   Name of treatment source _____ Date _____.
   Name, age, sex, color, marital status.
   Address, admission diagnosis, admission date.
   Treatment to date— _____ As _____ Bi.

Drug given at last treatment— _____ As _____ Bi.
Date last clinic visit.
Reasons for lapsing.
Dates of notification, method of notification.
Result:

A. Promise to return to clinic on _____ (date).
B. Under treatment at another source: Indicate _____.
C. Located, refuses further treatment.
D. Unable to locate—
    1. New address.
    2. Unable to trace; and be it further

Resolved, That the treatment source should be advised as to the results of the epidemiologic investigations to permit entry of the information on the medical record.

DIAGNOSTIC MEASURES

USE AND ADAPTABILITY OF THE DIRECT AND THE DELAYED DARK-FIELD EXAMINATION

Whereas the dark-field examination is a reliable laboratory method for the diagnosis of both primary and secondary syphilis; and

Whereas the dark-field examination is the only reliable laboratory method available for the routine diagnosis of syphilis during the early primary stage of the disease; and

Whereas the dark-field examination is a dependable diagnostic aid in differentiation of the lesions of early syphilis from those of other dermatologic conditions, and a positive dark-field examination confirms the diagnosis of early syphilis thus preventing delay in instituting treatment which arises from the wait for positive serologic findings; and

Whereas the delayed dark-field examination is of demonstrated efficiency in the diagnosis of primary syphilis when the attending physician is acquainted with the proper technic for the collection of serum from a suspected chancre but does not possess the necessary equipment; and

Whereas the delayed dark-field examination method makes it possible for a laboratory worker, thoroughly acquainted with the morphology of Spirochaeta pallida, to carry out the examination: Therefore be it

Resolved, That all State health departments should provide for direct and delayed dark-field diagnostic service; that all syphilis clinics should, so far as practicable, provide for direct dark-field diagnostic service; and that physicians should be encouraged to utilize direct or delayed dark-field examinations in the diagnosis of early syphilis.

ECONOMIC BASIS ON WHICH SEROLOGIC AND OTHER LABORATORY TESTS FOR THE DIAGNOSIS OF THE VENEREAL DISEASES ARE TO BE PERFORMED

Whereas the laboratory tests used in clinical management of the venereal diseases are of the greatest importance in the modern diagnosis of these diseases; and

Whereas it has become customary public health practice to provide without cost laboratory tests used in the control of the communicable diseases; and

Whereas emphasis upon the communicable character of the venereal diseases is most desirable from a public health standpoint: Therefore be it

Resolved, That health departments should, upon request of any licensed physician, clinic, or hospital in their jurisdictions, perform without charge accepted laboratory tests used in the control of the venereal diseases, including serologic tests for syphilis.

METHOD FOR DEMONSTRATION OF EFFICIENCY OF PERFORMANCE OF SEROLOGIC TESTS FOR SYPHILIS

In consideration of the widespread use of serologic tests for syphilis in public health and medical practice; and

Whereas laboratory workers are well aware of the difficulty of maintaining an efficient serologic test technic; and

Whereas such measures as adherence to conventional technic and periodic studies of the efficiency of performance of such tests are of material aid in maintaining their reliability: Therefore be it

Resolved, That those measures adopted during the Assembly of Laboratory Directors and Serologists at Hot Springs, Ark., October 1938 (Supplement No. 9 to Venereal Disease Information, U. S. Public Health Service, Washington, D. C., 1939) be applied, when the serologic work of the State laboratory is satisfactory, by all State health departments to all intrastate laboratories receiving governmental subsidies; and such measures are also recommended for all other serologic laboratories.

THE NEED FOR THE PROVISION OF SPECIAL VENEREAL DISEASE CONTROL LABORATORY SERVICES

Whereas laboratory examinations of spinal fluid are particularly important in the diagnosis and management of central nervous system syphilis; and

Whereas the Frei test is helpful in the diagnosis of lymphogranuloma venereum; and

Whereas the cultural method of identification of the gonococcus is of recognized value in the diagnosis and test of cure of gonococcus infections; and

Whereas few public health laboratories now provide for the above mentioned types of services: Therefore be it

Resolved, That public health laboratories should endeavor to provide for the appropriate laboratory examinations of spinal fluid to aid in the diagnosis of neurosyphilis; for the production of antigen for use in the Frei test and the intracutaneous test for chancroid; and for the cultural method of identification of the gonococcus.

CONTROL THROUGH TREATMENT

MINIMAL REQUIREMENTS FOR CLINICS

Whereas the clinic is one of the most important units in the venereal disease control program; and

Whereas the effectiveness of the clinic directly depends upon the efficiency with which it is operated: Therefore be it

Resolved, That the members of this conference do hereby suggest the following minimum requirements for clinic administration; and that every effort be made to attain these standards as rapidly as possible:

1. The clinic should be so located as to be of greatest service to the population to be served.
2. Evening clinic sessions should be designated and encouraged, to avoid financial loss to medically indigent employed patients and to meet other special needs.
3. Privacy, prompt service, and a pleasant cooperative attitude on the part of the clinic personnel are necessary and should be encouraged. In the crowded clinics with limited space, staggering of hours of attendance should be utilized.
4. Where practicable, polyclinics are preferable to ad hoc clinics.
5. The mechanical organization of the clinic should be such as to provide the maximum time for patient-physician consultation.
6. The facilities of the clinic should include standard minimum equipment necessary for the diagnosis and treatment of syphilis and gonorrhea as described by the Cooperative Clinical Group and the Public Health Service.
7. The personnel of the clinic should include, as an indispensable minimum, a director with special training in the management of the venereal diseases, in addition to adequate nursing, medical follow-up and clerical help.
8. The clinic should include lay and professional instruction and should cooperate with social and legal forces.

STANDARD TREATMENT FOR EARLY SYPHILIS

Whereas the patients with early syphilis (i. e., patients with syphilis of less than 4 years' duration) are usually healthy young adults free from complicating diseases; and

Whereas the manifestations of early syphilis and the extent of involvement of important body structures are surprisingly uniform; and

Whereas the response of patients with early syphilis to treatment is ordinarily uniform; and

Whereas an evaluation of treatment methods by two independent agencies, the Cooperative Clinical Group of the Public Health Service and the Medical Organization of the League of Nations, has established the worth of certain broad principles of therapy in early syphilis: Therefore be it

Resolved, That the continuous alternating scheme of therapy for syphilis of less than 4 years' duration, approved by the United States Public Health Service, is adopted by the members of this conference as standard treatment procedure in this stage of syphilis.

STANDARD TREATMENT FOR SYPHILIS IN PREGNANCY

Whereas the transmission of syphilis from the pregnant woman to her unborn child occurs five times out of six in untreated syphilitic women; and

Whereas the transmission of syphilis to the unborn child can be almost entirely prevented through the treatment of the mother during the gestation period; and

Whereas the beneficial results of treatment to the child are in direct proportion to the duration of treatment in the pregnancy period: Therefore be it

Resolved, That the members of this conference hereby recommend the adoption of all appropriate methods for the diagnosis of syphilis, including a routine serologic test, in every pregnant woman; and be it further

Resolved, That the members of this conference recommend that the scheme of treatment for syphilis in pregnancy consist of a minimum of 10 doses each of one of the arsenical and one of the bismuth compounds used in the treatment of syphilis, the administration of which is begun before the fifth month of gestation, beginning and ending treatment during the gestation period with arsenical therapy; and be it further

Resolved, That the systematic education of women as to the need to report to physicians or clinics for prenatal care earlier in pregnancy than is now the case is essential in the control of congenital syphilis; and be it further

Resolved, That postnatal observation and treatment if necessary in both the child and mother be continued at least for 6 months, or as long thereafter as may be indicated.

CONCENTRATION OF TREATMENT CONTROL MEASURES ON PATIENTS WITH COMMUNICABLE SYPHILIS

Whereas the public health control of syphilis is most effective in the early stage of this disease; and

Whereas many clinics will find more time to care for the early syphilis case-load if an organized effort is made to eliminate the over-treated patient with latent or late syphilis; and

Whereas over-treatment for late syphilis often results in serious damage to the patient: Therefore be it

Resolved, That the members of this conference deprecate the policy of treating patients with latent and late syphilis for months, years, or decades longer than is necessary, often at actual risk greater to the patient than that of his infection, and at wasteful use of public funds, and at the cost of crowding out early and potentially infectious patients for whom treatment will do much more good; and be it further

Resolved, That immediate steps be taken to discontinue this deplorable practice.

DISTRIBUTION OF FREE DRUGS BY THE HEALTH DEPARTMENT FOR THE TREATMENT OF THE VENEREAL DISEASES

Whereas the policy of distributing antisyphilitic drugs without charge to sources of treatment is one which promotes an effective campaign against syphilis; and

Whereas the distribution without cost of other biologic products is commonly accepted public health practice in the control of other communicable diseases when case reports are submitted to the health department; and

Whereas the private physician who treats syphilis assumes a public health obligation and should report all cases to the health department; and

Whereas the furnishing of such drugs is considered an important aid to the physician, and the reporting of cases is likewise of considerable aid to the health department: Therefore be it

Resolved, That the members of this conference approve of the distribution without charge of an accepted trivalent arsenical compound and an accepted bismuth compound by all health departments to all treatment sources (except special State and Federal institutions) upon request, provided only that such treatment sources cooperate with the health department in submitting morbidity and other reports and are duly licensed in the State to administer such drugs.

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PROVISION OF CONTINUOUS CARE FOR THE TRANSFERRING OR TRANSIENT PATIENT

Whereas the continuous treatment and observation of the patient with syphilis is of the utmost importance in the public health control of this disease; and

Whereas many administrative difficulties are encountered in the transfer of patients from one treatment source to another, or in the administration of effective treatment to the transient patient: Therefore be it

Resolved, That all health departments and clinics cooperating in the present campaign against the venereal diseases be supplied with a satisfactory form for recording essential clinical data and treatments, to be used in the transfer of such patients from clinic to clinic; and be it further

Resolved, That such transfer forms should include the following minimal data:

1. Identification of the patient: Admission age; sex and race, admission and transfer date; basis for original diagnosis; stage of syphilis at time of transfer.
2. Transcript of all treatment in the transferring clinic with the periods during which it was administered; the patient's clinical and serologic reactions to the therapy; an indication as to whether or not he was previously treated before admission to the transferring clinic.
3. The signature of the patient, provided the State law requires this for release of the information; and be it further

Resolved, That the responsibility of the original clinic does not end until it has taken pains to give the patient being transferred exact instructions as to the clinic or physician to which he should report next, to send independently to such clinic or physician a copy of the record which is also furnished to the patient, and to send a confidential notification of these arrangements to the health department serving the location to which the patient intends to move; and be it further

Resolved, That the clinic or physician to which the patient transfers notify the transferring clinic or physician of the patient's arrival and resumption of treatment; and, if the patient does not arrive within a reasonable time, the receiving clinic or physician should notify the original clinic or physician of this fact.

EFFECTIVENESS OF THE MOBILE TREATMENT UNIT

Whereas the mobile treatment unit has been demonstrated to be an effective and economical measure in controlling syphilis, in carrying on general public health measures in rural areas, and as an important measure in public health education; and

Whereas the cost (including depreciation) of operating such a mobile unit approximates about one-half of the salary of the physican in charge of the unit, and permits the technical team attached to the unit to serve several times as many people as would be the case if stationary health clinics were organized in the same area: Therefore be it

Resolved, That the members of this conference recommend the use of mobile treatment units for such health activities in rural counties wherever the prevalence of syphilis exceeds the average.

EFFECTIVE METHODS FOR SUPPRESSION OF QUACK AND DRUG STORE TREATMENT

Whereas the practice in many States and localities of permitting quacks and drug store clerks to prescribe treatment for persons infected with syphilis or gonorrhea greatly handicaps the effective control of these diseases: Therefore be it

Resolved, That the members of this conference recommend the enactment of the following legislation by all State legislatures:

1. That it shall be unlawful for any person, firm, or corporation to advertise within the State of _____ any medicine or remedy by means of a prescription or otherwise of a treatment, cure, or preventive for the venereal diseases:

   Provided, this section shall not apply to advertising of drugs in medical trade periodicals or scientific, medical, or dental journals, or literature mailed direct to physicians, hospitals, or firms engaged in the sale of drugs and medicinal appliances to physicians or pharmacists.

2. That it shall be unlawful for any person, firm, or corporation to sell any drug or medicine to any person other than a dealer, druggist, hospital, or physician for the cure or alleviation of the venereal diseases without a written order or prescription written for the person for whom the drug or medicine is to be delivered and signed by a physician authorized to practice medicine in the State of _____.

CLINICAL SERVICE FOR THE CONTROL OF THE VENEREAL DISEASES IN RURAL AND OTHER ISOLATED AREAS

Whereas individuals in many areas, especially the rural South, do not now have access to physicians or clinic facilities for the diagnosis and treatment of syphilis and gonorrhea; and

Whereas the full-time, trained, traveling clinician may be found to be of distinct value in such areas to operate clinics and to work with private physicians in the management of clinics, especially where the prevalence of the venereal diseases has been established to be greater than average; and

Whereas stationary treatment and diagnostic centers may be conveniently located to serve population groups advantageously so that a minimum of transportation difficulties exist; and

Whereas the establishment of clinic facilities in areas where local health service does not exist has been found to be advantageous: Therefore be it

Resolved, That further studies and demonstrations of this and other methods to meet such needs be encouraged, closely observed, and reported upon.

CONSULTATION SERVICE FOR PHYSICIANS IN CLINICS AND IN PRIVATE PRACTICE

Whereas the provision of an effective consultation service is of primary importance in the control of syphilis and gonorrhea: Therefore be it

Resolved, That State and municipal health departments organize a consultation service along the following lines:

1. Diagnostic service in a polyclinic hospital to which clinic patients needing special clinical or laboratory examinations or hospitalization may be referred.
2. A peripatetic consultation service whereby a special consultant or, where circumstances permit or make it advisable, the venereal disease control officer, visits health department clinics regularly to advise with reference to special diagnostic and therapeutic problems.
3. A consultation service by mail or telephone in which diagnostic and therapeutic problems may be stated by the physician to the consultant.

MEASURES FOR THE CONTROL OF SYPHILIS IN INDUSTRY

Whereas it has been established that the application of certain measures designed for the control of syphilis in industry contributes much to the effectiveness of a general venereal disease control program as well as to the health of the worker, efficiency of industry, and general well-being of the community; and

Whereas the measures for the applicant for employment usually applied to attain this end are—

1. Routine blood testing before employment.
2. Employment without prejudice of individuals with syphilis provided adequate treatment is taken.
3. As soon as open lesions of early syphilis are healed, and provided the individual continues to take adequate treatment, the applicant is to be employed without prejudice.
4. The employer is justified in refusing employment to applicants who have the late crippling manifestations of syphilis which may render them industrial hazards or poor retirement risks; and

Whereas the measures for the old employee usually applied to attain this end are—

1. Routine periodic blood testing of all employees.
2. Continued employment without prejudice of individuals with syphilis, provided adequate treatment is taken.
3. Provisions for occupational readjustments or retirement of employees who develop disabling manifestations of late syphilis.
4. Educational work in the control of syphilis among employee and management groups: Therefore be it

Resolved, That the members of this conference endorse these plans for the control of syphilis in industry; and be it further

Resolved, That health departments, labor organizations, and industrial leaders cooperate to encourage and to adopt such measures.

PROVISION IN PUBLIC MENTAL HOSPITALS OF FREE NONSPECIFIC THERAPY FOR VOLUNTARY PATIENTS WITH CHEMOTHERAPEUTIC-RESISTANT ASYMPTOMATIC NEUROSYPHILIS

Whereas the development of symptomatic central nervous system syphilis cannot be prevented in all cases by conventional chemotherapeutic treatment of patients with early syphilis; and

Whereas it is difficult for most health departments to arrange for the administration of nonspecific therapy to chemotherapeutic-resistant patients with asymptomatic neurosyphilis; Therefore be it

Resolved, That the members of this conference deprecate the policy of mental hospitals in failing to admit voluntary patients with chemotherapeutic-resistant asymptomatic neurosyphilis; and strongly urge that this measure be adopted—a measure which, if undertaken, will greatly decrease the incidence of symptomatic central nervous system syphilis in the United States.

PROVISION IN PUBLIC HOSPITALS OF FREE NONSPECIFIC THERAPY TO VOLUNTARY PATIENTS WITH CHEMOTHERAPEUTIC-RESISTANT SYPHILIS OTHER THAN NEUROSYPHILIS

Whereas certain cases of acquired and congenital syphilis cannot always be successfully treated by conventional chemotherapeutic measures but can be aided by nonspecific therapy: Therefore be it

Resolved, That the members of this conference recommend that public hospitals admit voluntary patients with chemotherapeutic-resistant syphilis for nonspecific therapy, provided such hospitals are equipped to administer such treatment.

CASE-FINDING AND CASE-HOLDING

CONTACT-TRACING AND THE SEROLOGIC SURVEY AS CASE-FINDING MEASURES

Whereas the actual finding of cases of syphilis is of essential importance to the effectiveness of a control program; and

Whereas all means available which may be productive in this regard should be utilized: Therefore be it

Resolved, That it is the opinion of the members of this conference that both case-finding measures and the serologic survey are of value, but that suitable emphasis should be placed upon the method best fitted to the problem in any given population.

LAPSED PATIENT FOLLOW-UP; CONTROL OF THE IGNORANT AND RECALCITRANT PATIENT WITH COMMUNICABLE VENEREAL DISEASE

Whereas continuity is one of the most important characteristics of the schedules of treatment for syphilis and gonorrhea, and

Whereas every reasonable attempt should be made to keep the patient with early syphilis and with gonorrhea under continuous treatment and observation; Therefore be it

Resolved, That every attempt be made by properly trained personnel to teach the patient the manifestations of the venereal diseases and their danger to the public health and to encourage him to seek treatment voluntarily; and be it further

Resolved, That should the persuasive method fail due to the inability of the patient to comprehend the importance of the problem or to his unwillingness to take treatment because of recalcitrance, as a last resort, the patient be forcibly isolated, following the same procedure for the protection of the community as with any other communicable disease.

PREMARITAL LAWS IN THE CONTROL OF SYPHILIS

Whereas the incidence of syphilis is highest in the age group from 15 to 30, which is also the age group within which most marriages take place; and

Whereas any step toward the prevention of syphilis within marriage would be of inestimable benefit to the institution of marriage and the preservation of the race: Therefore be it

Resolved, That, as soon as favorable public opinion has been created and proper laboratory facilities are available, all States should enact sound laws, and provide adequate appropriations for their administration, requiring every applicant for a marriage license to submit to a clinical examination by a physician and to a serologic examination performed by a laboratory, approved by the State department of health, for evidence of syphilis, and to present to the licensing authority a certificate from such physician stating that, in his opinion, based on the results of such clinical and serologic examinations, the applicant is either not infected with syphilis, or, if so infected, is not in a stage of the disease which is communicable to the marital partner.

PRENATAL LAWS IN THE CONTROL OF SYPHILIS

Whereas many thousand children are born alive every year with congenital syphilis and an almost equal number are aborted or born dead because of this disease, and

Whereas congenital syphilis can be prevented in 90 cases out of every hundred if the disease is discovered in the mother before the fifth month of pregnancy and adequately treated thereafter: Therefore be it

Resolved, That as soon as a favorable public opinion has been created and proper laboratory facilities are available all States should enact sound laws, and provide adequate appropriations for their administration, requiring licensed physicians and every other person permitted by law to attend upon pregnant women to take or cause to be taken specimens of blood from every pregnant woman attended by them as soon as practical after the first visit and to submit such specimens to a laboratory approved by the State department of health for standard tests for syphilis; and be it further

Resolved, That such laws should contain a provision requiring the inclusion in the birth certificate of a statement by the doctor or midwife delivering the child whether such blood test was made and if so, when.

INFORMATIVE PROGRAM AMONG PHYSICIANS

GAINING THE INTEREST OF YOUNG PHYSICIANS IN VENEREAL DISEASE CONTROL

Whereas the graduate of the medical school has an important part to play in the control of the venereal diseases in the years following his graduation, not only in private practice but also in their public health control; and

Whereas the selection of new venereal disease control officers and clinicians must be made from the graduates of medical schools in the normal replacement of such personnel: Therefore be it

Resolved, That health officers with suitable personality, experience, and knowledge be delegated by health departments to seek out eligible young physicians from among hospital internes, and through special conferences, specialized instruction, or by circularization with current informative material develop the interest and effectiveness of these young physicians in the field of venereal disease control; and be it further

Resolved, That the members of this conference request the Surgeon General of the Public Health Service, the Chairman of the Conference of State and Provincial Health Officers and the respective State health officers to emphasize by letter the importance of training in the clinical management and public health control of the venereal diseases to the faculties of medical schools throughout the United States in an attempt to develop a more effective curriculum.

DISSEMINATION OF INFORMATIVE LITERATURE

Whereas one of the chief mediums for the stimulation of interest of private physicians in venereal disease control is through the dissemination of informative literature; and

Whereas the assistance of well-informed physicians in private practice is of vital importance in the control of the venereal diseases: Therefore be it

Resolved, That the dissemination of informative literature is essential and that this material be specially selected to aid the physician in practice and to secure his active cooperation in the public health control of the venereal diseases; and be it further

Resolved, That in the preparation of informative material special attention be given to the following fundamental principles:

1. The material should be interesting, scientific, and brief.
2. Reprints and other special publications should be distributed regularly and should deal with special problems of diagnosis, treatment, and after-care, which the general practitioner frequently meets in his routine work.
3. Professional groups should receive from time to time copies of material used in the education of citizens, in order that the former may be encouraged to supplement, through personal instruction, the influence of the pamphlets on the public.
4. There should be follow-up consultations with private physicians to secure application of the ideas promulgated by the health department.

ENCOURAGEMENT OF PHYSICIAN'S ATTENDANCE AT MEDICAL SOCIETY MEETINGS

Whereas the regular attendance of physicians at medical society meetings affords an opportunity for professional improvement by becoming familiar with the newer advances in the medical sciences; and

Whereas it is recognized that the practicing physician is expected to give his patient the benefits of accepted scientific methods in the diagnosis and treatment of disease; and

Whereas active particpation on the part of each member in the affairs of the local medical society promotes the more widespread utilization of scientific procedures and regular attendance: Therefore be it

Resolved, That physicians be encouraged in the regular attendance of local medical society meetings by the president of the American Medical Association, the president of the State and district medical societies, the State and local health officers; and be it further

Resolved, That the local medical society make provision for the active participation of each member in performing some service in connection with the organization, administration, and conduct of the society, and in the planning, development, and participation of programs and committee service; and be it further

Resolved, That the members of this conference particularly recommend that the above measures be applied to interest physicians in the problems of the clinical management of the venereal diseases.

PUBLIC EDUCATIONAL MEASURES

SCOPE, CONTENT, AND DISTRIBUTION OF POPULAR VENEREAL DISEASE EDUCATIONAL MATERIAL

Whereas a knowledge on the part of the lay public of the facts about the venereal diseases is essential to the success of any venereal disease control program both from the point of view of the development and support of adequate facilities and the cooperation of the individual patient; and

Whereas such facts must reach the persons most concerned in an easily understood and attractive form; Therefore, be it

Resolved, That the importance and responsibility for the development of a well integrated, broad public educational program be recognized by all health departments; and be it further

Resolved, That all available mediums of communication, such as the press, radio, motion and slide pictures, streetcar placards, posters, pamphlets, exhibits, and all groups and organizations in the population such as trade groups, unions, women's clubs, youth groups, be utilized in the dissemination of the facts about the venereal diseases; and be it further

Resolved, That in the preparation of informative material, special attention be given to the following fundamental principles:

1. The material should be scientifically accurate.
2. The material should be attractively designed, brief with only one or two major ideas, and written for appeal to the audience for which it is to be used and with consideration of the audience's educational level, preconceptions, and customs.
3. In developing materials, consideration should be given to the problem of distributing them in the most economical and effective manner to the groups needing them; and be it further

Resolved, That the United States Public Health Service be asked to cooperate with health, educational, and voluntary agencies in disseminating information with regard to the educational activities and technics in use throughout the United States in order to develop more effective educational programs in each community and to aid in the evolvement of new and more efficient types and technics.

SHOULD SEX EDUCATION BE ENCOURAGED BY THE HEALTH OFFICER

Whereas there is a growing recognition of the importance of adequate sex instruction and preparation for marriage and family life; and

Whereas parents, teachers, the clergy, and others concerned with such education benefit by the active cooperation and assistance of public health and medical authorities; and

Whereas well-planned and successful teaching of this character is of benefit to the broad program of mental and physical health: Therefore be it

Resolved, That health authorities should encourage the development of a sound and adequate sex education program.

ADMINISTRATIVE PROBLEMS

COORDINATION AND INTEGRATION OF THE VENEREAL DISEASE CONTROL PROGRAM IN THE GENERAL HEALTH PLAN

Whereas the effective administration of the venereal disease control program is most important in the campaign against these diseases; and

Whereas the proper delegation of authority to responsible staff members by the State or local health officer is conducive to the most effective type of administrative practice: Therefore be it

Resolved, That—

1. Venereal disease control work should be integrated or performed in close liaison with the preventable disease unit of the health department.
2. Venereal disease control work should be directed under a separate division or subdivision having in either instance at least as high a degree of autonomy as tuberculosis control, maternal and child health work, malaria control, and other special health activities.
3. The program should be directed by a full-time venereal disease control officer wherever the total population of the area served exceeds 500,000, or whenever the use of such an officer is deemed advantageous in areas of smaller populations.
4. To be most effective, venereal disease control service should be correlated with all other divisions and activities of the health department and particularly with the laboratory, maternal and child care, and industrial hygiene.

BASES FOR APPORTIONMENT OF VENEREAL DISEASE CONTROL FUNDS

Whereas the proportion of time given by personnel in, and the amount of money allotted by health departments to, the control of the venereal diseases are of primary importance in the campaign; and

Whereas the equable allotment of funds by Federal, State, and local governments is necessary in the provision of successful control measures: Therefore be it

Resolved, That—

1. Each State and local health department shall carefully consider a venereal disease control plan to secure for the public adequate protection against the spread of these diseases by infected individuals, and for the individual patient adequate treatment, skilled medical care, and maximum privacy.
2. The apportionment of funds should follow some definite system such as the following:
   a. The relative prevalence and importance of the venereal diseases in relation to all communicable diseases in the area.
   b. The financial need existing in each area as determined by recognized economic indices.
   c. The ability of the respective areas to utilize funds effectively; and be it further

Resolved, That in the allotment of funds to, and the provision of service for, the control of the venereal diseases due regard be given to the integration and coordination of local, State, and Federal programs in order that the work may be made as uniform as practicable under the varying social and economic conditions existing throughout the Nation.

THE ADVISORY COMMITTEE AS A SUPPORTING GROUP FOR THE VENEREAL DISEASE CONTROL PROGRAM

Whereas there are numerous activities pertaining to venereal disease control which relate to medicine, public health, public welfare, and sociology; and

Whereas the venereal disease control officer should avail himself of the very best type of consultation in his community: Therefore be it

Resolved, That each venereal disease control officer utilize the aid of a special venereal disease council or a section of the general health council composed of representative members of professional and civic groups, and other persons informed on the need for, or provision of, venereal disease control services; and be it further

Resolved, That the functions of this council be to maintain continuous public interest, to advise with reference to health department policy, and to assist in securing adequate funds from appropriating bodies or from private philanthropies, or from both such sources.

VOLUNTARY AGENCY SUPPORT OF THE VENEREAL DISEASE CONTROL PROGRAM

Whereas because of their tragic nature and widespread prevalence, the solution of problems created by syphilis and gonorrhea and other so-called venereal diseases is of vital importance to the health and welfare of the American people; and

Whereas action by National, State, and local governmental agencies only is not enough to deal with the complex educational, recreational, and environmental influences which are of assistance in their prevention or control; and

Whereas governmental agencies cannot, in many instances, deal with such matters as the promotion of needed venereal disease control legislation, appropriations, the repression of prostitution, long-time character building programs for youth; and

Whereas there is a need for a strong continuing national agency through which citizen interest generally can make itself felt in supplementing the activities of governmental agencies in this field: Therefore be it

Resolved, That the State and local health authorities join with the United States Public Health Service and other official agencies in welcoming and supporting the widest possible development of the work of the American Social Hygiene Association, its affiliates, and other voluntary agencies, so organized as to deal with this series of health, welfare, and educational problems.

QUALIFICATIONS OF PERSONNEL

QUALIFICATIONS OF THE VENEREAL DISEASE CONTROL OFFICER ADOPTED BY THE CONFERENCE OF STATE AND TERRITORIAL HEALTH OFFICERS

Whereas an effective campaign against the venereal diseases is largely dependent upon its direction by a thoroughly qualified venereal disease control officer: Therefore be it

Resolved, That the basic educational requirements and special qualifications of venereal disease control officers shall be those adopted by the Conference of State and Territorial Health Officers on April 25, 1939, to wit:

1. The earned degree of doctor of medicine from a reputable medical school and eligibility to examination for medical licensure in the State where service is to be rendered.
2. Not less than 1 year of general clinical experience gained preferably in a hospital of acceptable standards.
3. The satisfactory completion of not less than 1 academic year of work in a recognized postgraduate school of public health, or in lieu of this special training, 2 years of full-time public health work.
4. A period of at least 6 months' intensive training in the clinical management of the venereal diseases in a well-organized postgraduate course, or its equivalent (not less than 1 year of work in a recognized school of public health) if instruction in the clinical management of the venereal diseases constitutes a stipulated part of the course of training in the school of public health.

MINIMAL QUALIFICATIONS FOR CLINICIANS, CLINIC NURSES, AND MEDICAL SOCIAL WORKERS

Whereas the qualifications and experience of physicians, nurses, and medical social workers who serve in venereal disease clinics are of the greatest importance in their efficient management: Therefore be it

Resolved, That it is the sense of this conference that it is highly desirable for the qualifications of physicians serving in such clinics to be:

1. An earned degree of doctor of medicine from a reputable school and eligibility to examination for medical licensure in the State in which he is to serve. The physician selected, if not already licensed to practice within the State, should be licensed at the meeting of the board of medical examiners next succeeding his appointment.
2. Not less than 1 year of general clinical experience gained preferably in a hospital of acceptable standards.
3. A period of at least 6 months' intensive training in the clinical management of the venereal diseases in a well-organized postgraduate course; and be it further

Resolved, That it is the sense of this conference that it is highly desirable for the qualifications of a nurse serving in such clinics to be:

1. A graduate from an accredited school of nursing meeting the minimum requirements set by State law; preferably such school of nursing should be connected with a general hospital having a daily average of 100 or more bed patients, and the necessary affiliations to provide a program of study which should include instruction and experience in obstetric, pediatric, orthopedic, and communicable disease nursing, including the control of gonorrhea, syphilis, and tuberculosis.
2. Eligibility for registration in the State in which she is to serve.
3. Not less than 3 months' and preferably 6 months' experience in a venereal disease clinic of acceptable standards; or, in lieu thereof, not less than 1 year of general nursing experience after graduation from nursing school in a hospital of acceptable standards; and be it further

Resolved, That it is the sense of this conference that it is highly desirable for the qualifications of a medical social worker to be:

1. Graduation from an accredited course in medical social work in an approved school of social work, and
2. One year's supervised experience in the practice of medical social work in a recognized social service department in a hospital or clinic which has an active syphilis control department.

Or in lieu thereof—

1. Graduation from a 2-year course in an approved school of social work, and
2. Three years' supervised experience in the practice of medical social work in a recognized social service department in a hospital or clinic, 1 year of the experience to be in a syphilis control program; and be it further

Resolved, That in the selection of the above personnel consideration should be given to personal qualifications, and only those persons who

have tactful personalities and a particular interest in the venereal diseases and in public health be selected.

MINIMAL QUALIFICATIONS OF THE PUBLIC HEALTH NURSING CONSULTANT

Whereas the public health nursing aspects of a venereal disease control program are most effective when included as an integral part of the family health program of the community public health nurse; and

Whereas until all public health nurses have had an adequate preparation in venereal disease control, the service of a qualified public health nursing consultant is essential: Therefore be it

Resolved, That the public health nursing consultant in venereal disease control should possess the following qualifications:

1. An earned degree of bachelor of science or bachelor of arts from a reputable college or university.
2. A graduate from an accredited school of nursing meeting the minimum requirements set by State law and connected with a general hospital having a daily average of 100 or more bed patients, and the necessary affiliations to provide a program of study which should preferably include instruction and experience in obstetric, pediatric, orthopedic, and communicable disease nursing, including the control of gonorrhea, syphilis, and tuberculosis, and eligible for registration in the State in which she is practicing.
3. Completion of at least 1 year's approved postgraduate study in public health nursing carrying regular academic credit.
4. Experience of at least 2 years in a general public health agency which provides supervision by qualified public health nursing personnel and preferably experience of at least 1 year as a general supervisor.
5. At least 3 months of advanced preparation in applied venereal disease epidemiology at an educational institution which meets approved standards.

POSTGRADUATE TRAINING OF VENEREAL DISEASE CONTROL OFFICERS, CLINICIANS, COOPERATING PRIVATE PHYSICIANS, AND OTHER PUBLIC HEALTH AND SCIENTIFIC PERSONNEL

Whereas the postgraduate training of health officers, clinicians, cooperating private physicians, nurses, medical social workers, and laboratory personnel is one of the most effective methods of instructing such personnel; and

Whereas complete familiarity of such personnel with the most modern procedures for the public health control and clinical management of the venereal diseases in their respective fields is conducive to the best type of campaign: Therefore be it

Resolved, That State health officers are earnestly requested to nominate a sufficient number of capable young physicians, nurses, medical social workers, and laboratory workers to take one of the numerous postgraduate training courses now available; and be it further

Resolved, That the number of such personnel nominated to postgraduate training courses by the State health officer be sufficient to meet the needs in the respective fields of the rapidly expanding venereal disease control program in a given State.

ADDENDUM

Suggested Report Forms

Name _____ Pat. Record No. _____

Address _____ Informant No. _____

City _____ County _____ Color ____ Sex ____ Age ____

SYPHILIS

Date of Onset _____

ACQUIRED:
- Primary ☐
- Early: Secondary ☐
- Early: Latent (less than 4 yrs.) ☐
- Late: Late symptomatic ☐
- Late: Latent (more than 4 yrs.) ☐

CONGENITAL: *Specify* ☐

Date of Onset _____

GONORRHEA (Genitalia ☐ (Eyes ☐ (Other ☐

CHANCROID ☐

GRANULOMA INGUINALE ☐

LYMPHOGRANULOMA VENEREUM ☐

Laboratory: Report as
+ Positive ± Doubtful
- Negative o Not done

- Darkfield ☐
- Blood Test ☐
- Smear ☐
- Culture ☐
- Frei ☐
- D'melcos ☐

Previous treatment: No ☐ Yes ☐ Give amount _____

Is patient now pregnant? _____ Month of expected delivery _____

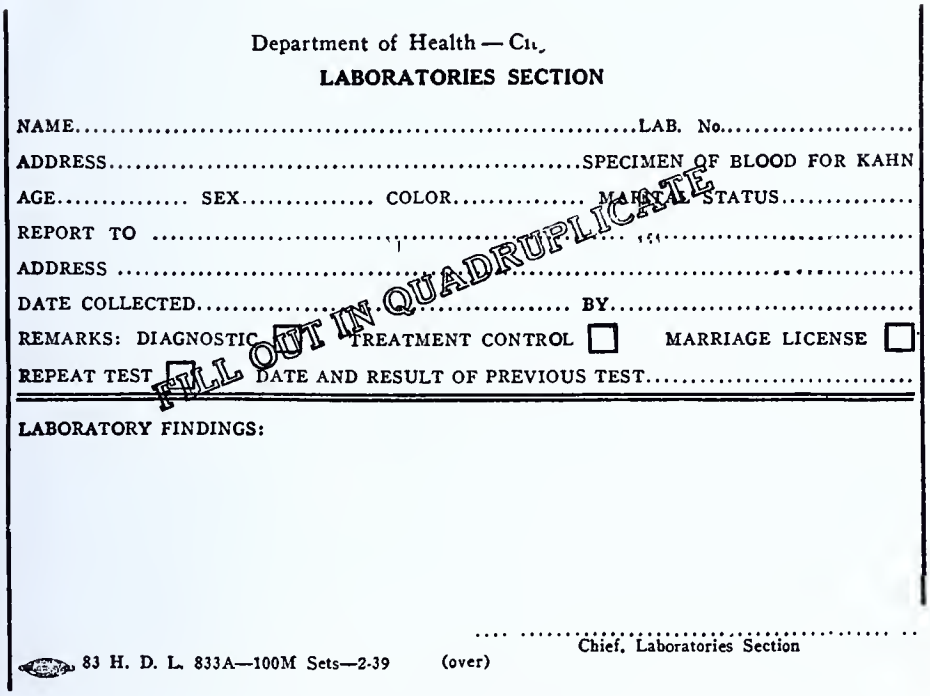
Physician's Case Report
_____ State Dept. of Health
in cooperation with
U. S. Public Health Service
VM-1041

Signed _____ M. D.

Address _____

Date of Report _____

FIGURE 1.—Physician's case report to State department of health.



Department of Health — Ci[illegible]

LABORATORIES SECTION

REPORTED

NAME.....LAB. No.....

ADDRESS.....SPECIMEN OF BLOOD FOR KAHN

AGE..... SEX..... COLOR..... MARITAL STATUS.....

REPORT TO .....

ADDRESS .....

DATE COLLECTED..... BY.....

REMARKS: DIAGNOSTIC ☐ TREATMENT CONTROL ☐ MARRIAGE LICENSE ☐

REPEAT TEST ☐ DATE AND RESULT OF PREVIOUS TEST.....

FILL OUT IN QUADRUPLICATE

LABORATORY FINDINGS:

DATE RECEIVED

..... Chief, Laboratories Section

83 H. D. L. 833A—100M Sets—2-39 (over)

FIGURE 2.—Report of laboratory findings.

EXPLANATION OF LABORATORY REPORT

POSITIVE—Both a Kahn and a Wassermann Test have been performed on this specimen. Both are positive or one is positive and the other strongly suggestive. Unless the clinical diagnosis or history definitely indicate syphilis, no patient should be treated for syphilis on the basis of a single specimen. CONFIRM THIS RESULT BY A REPEAT SPECIMEN IF THERE IS ANY DOUBT AS TO CLINICAL DIAGNOSIS.

DOUBTFUL—The two tests used give an inconclusive result. This may or may not be due to the presence of syphilitic infection. This result calls for a careful clinical check-up and a repeat specimen.

NEGATIVE—The Kahn Test on this specimen gives no serologic evidence of syphilis. However, a negative result does not necessarily exclude the presence of syphilis, and in a patient under treatment, it does not necessarily imply cure.

FIGURE 2a.—Reverse of figure 2.

RECORD NO: SURNAME FIRST NAME MAIDEN NAME ADMISSION DIAGNOSIS

AGE SEX COLOR S M W D S MARITAL STATUS DATE OF ADMISSION

ADDRESS (1) (2) (3)

I HISTORY AND PHYSICAL EXAMINATION

EXAMINED BY: DATE

PREVIOUS TREATMENT: ARSENICAL HEAVY METAL (GIVE DETAIL ON TREATMENT RECORD — PENICILLIN, SULFA)

BEGINNING ENDING

PREGNANCIES (YEARS OF) LIVE BIRTHS

MISCARRIAGES OR STILLBIRTHS

REASON FOR CLINIC ATTENDANCE: VOLUNTEER EMPLOYMENT PREMARITAL PREGNANCY ROUTINE TEST REFERRED BY

PRIMARY LESION (LOCATION) DATE

SECONDARY LESIONS DATE

LATE MANIFESTATIONS: TYPE,

ONSET OF SYMPTOMS DURATION:

FIRST POSITIVE SEROLOGY: DATE WHERE?

LAST SEROLOGIC TEST: KAHN KLINE DATE

PHYSICAL EXAMINATION.

HEIGHT WEIGHT GENERAL HEALTH

SKIN (ERUPTIONS, ETC.) MENTAL STATUS

MUCOUS MEMBRANES

LYMPHATIC SYSTEM

EYES

CARDIOVASCULAR: BLOOD PRESSURE /

HEART SOUNDS

HEART BORDERS

LUNGS

GENITALIA

REFLEXES: PUPILLARY DEEP TENDON

ROMBERG OTHER

COEXISTING DISEASE.

II SOCIAL AND EPIDEMIOLOGICAL

DATE OF FIRST INTERVIEW: WORKER

MARITAL STATUS (GIVE DATES)

HOUSEHOLD ROSTER	SEX	AGE	RELATIONSHIP

SEXUAL CONTACTS

				UNTRACEABLE	EXAMINED	CASE FOR TREATMENT UNDER DR.
1) NAME	AGE	COLOR	SEX			
ADDRESS	DATE OF CONTACT					
2) NAME	AGE	COLOR	SEX			
ADDRESS	DATE OF CONTACT					
3) NAME	AGE	COLOR	SEX			
ADDRESS	DATE OF CONTACT					
4) NAME	AGE	COLOR	SEX			
ADDRESS	DATE OF CONTACT					
5) NAME	AGE	COLOR	SEX			
ADDRESS	DATE OF CONTACT					
6) NAME	AGE	COLOR	SEX			
ADDRESS	DATE OF CONTACT					

CASE HOLDING EFFORTS (HOME VISITS)

1.
2.
3.
4.
5.
6.

III SPECIAL EXAMINATIONS

EYE

CORNEA O.D. O.S.

SCLERA O.D. O.S.

E.O.M. O.D. O.S.

VISUAL ACUITY O.D. O.S.

OPHTHALMOSCOPIC MEDIA O.D. O.S.

FUNDI O.D. FIELDS O.D.

O.S. O.S.

DIAGNOSIS: EXAMINED BY

CARDIOVASCULAR SYSTEM

PULSES: RATE CHARACTER

BLOOD PRESSURE: ARM: RIGHT / LEFT /

LEG: RIGHT / LEFT /

HEART PMI

RIGHT BORDER

LEFT BORDER

RMD

AUSCULTATION.

DIAGNOSIS. EXAMINED BY.

NEUROLOGICAL AND PSYCHIATRIC

DIAGNOSIS. EXAMINED BY.

VM 1042

III SPECIAL LABORATORY (CROSS REFERENCE IN PROG. NOTES)

DARKFIELD.

DATE	SOURCE OF SPECIMEN	NO. SPECIMENS EXAMINED	RESULT

HEMATOLOGY:

DATE	RED COUNT	W.B.C.	DIFFERENTIAL COUNT	PLATELET COUNT	ICTERUS INDEX	OTHER

KIDNEY FUNCTION OR SPECIAL URINE

DATE	

RE-EXAMINATIONS OR OTHER EXAMINATIONS

1) DATE

2) DATE

3) DATE

4) DATE

FIGURE 3.—Physician's treatment record for syphilis.

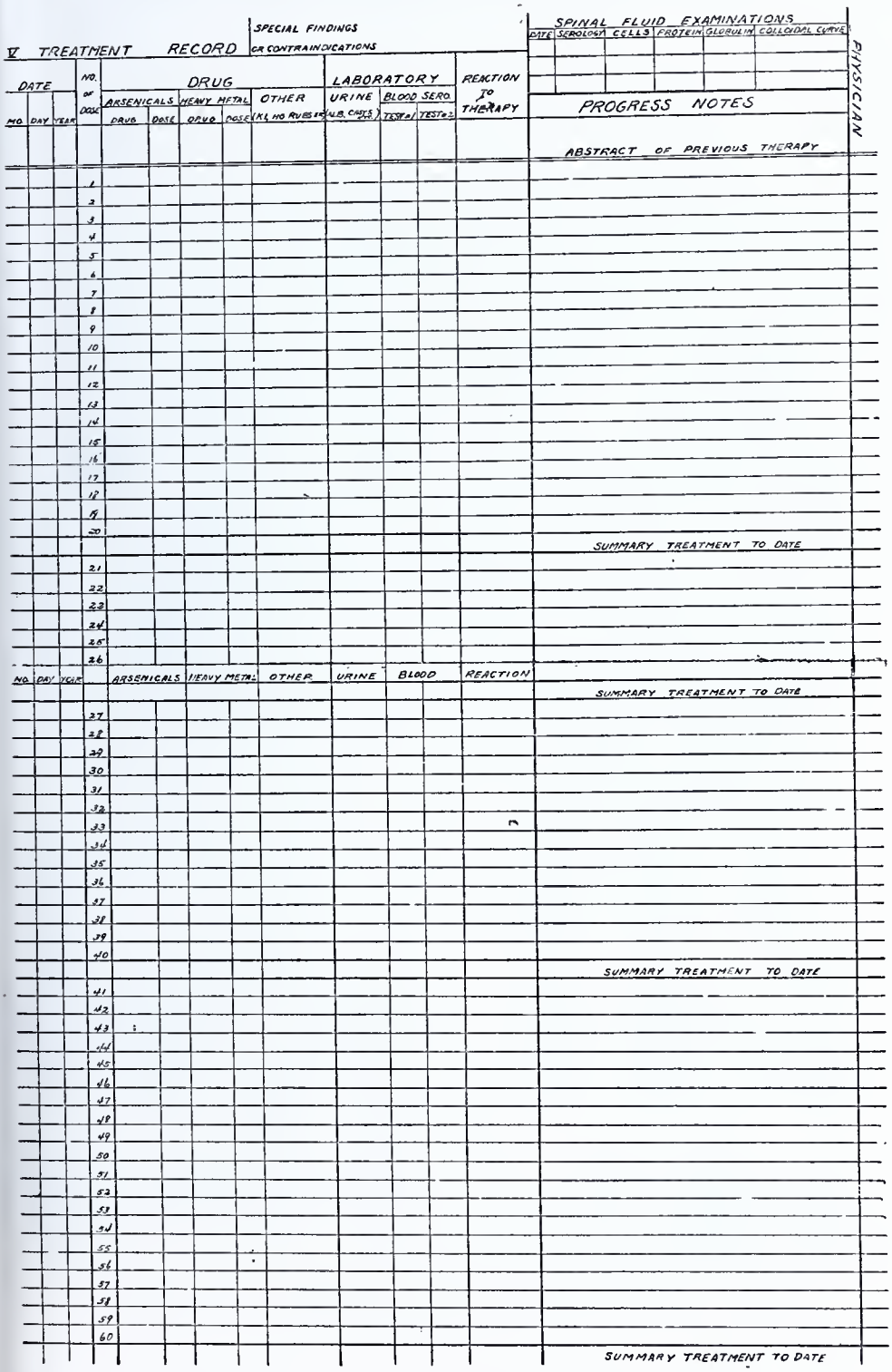


FIGURE 3a.—Reverse of figure 3.

Case Number _____ Admission Date _____

I. IDENTIFICATION

Name _____ Address _____

Age _____ Marital Status Work

Race White ☐ Single ☐ Widowed ☐ Light ☐
Negro ☐ Married ☐ Divorced ☐ Average ☐
Other ☐ Separated ☐ Heavy ☐

II. PREVIOUS GONORRHEA

No ☐ Yes ☐ Date _____

Diagnosis (Specify using code.) _____

III. PRESENT GONORRHEA - ADMISSION

Date exposed _____ Days of incubation _____ Days duration of infection _____

Contacts	Name	Address	Age	Sex	Color	Result - Record No. if under treatment
1.						
2.						
3.						
4.						

Previous treatment this infection Yes ☐ Description _____
No ☐ _____

Admission Physical Examination this infection (Check normal or abnormal)

	Normal	Abnormal
Tyson's gland	☐	☐
Extraurethral ducts	☐	☐
Epididymis Rt	☐	☐
Lt	☐	☐
Vas deferens Rt	☐	☐
Lt	☐	☐
Anus	☐	☐
Cowper's glands	☐	☐
*Prostate	☐	☐
*Seminal vesicles Rt	☐	☐
Lt	☐	☐
Joints	☐	☐
Lymphatic glands	☐	☐
Other (specify)	☐	☐

*Defer examination when contraindicated

Diagnosis:
Code
10 - Anterior urethritis ☐
20 - Anterior-posterior urethritis ☐
30 - Complications (not specified) ☐
31 - Follicalitis ☐
32 - Cowperitis ☐
33 - Epididymitis ☐
34 - Prostatitis ☐
35 - Seminal vesiculitis ☐
36 - Arthritis ☐
37 - Eye ☐

SYPHILIS	Tests Positive	Negative
Admission		
Blood	☐	☐
Darkfield	☐	☐
Three months after admission		
Blood	☐	☐
Clinical Manifestations _____		

Remarks _____

Patient history and treatment record - Gonorrhea (male)
U. S. Public Health Service - Field Study

FIGURE 4.—Patient's history and treatment record—Gonorrhea (male).

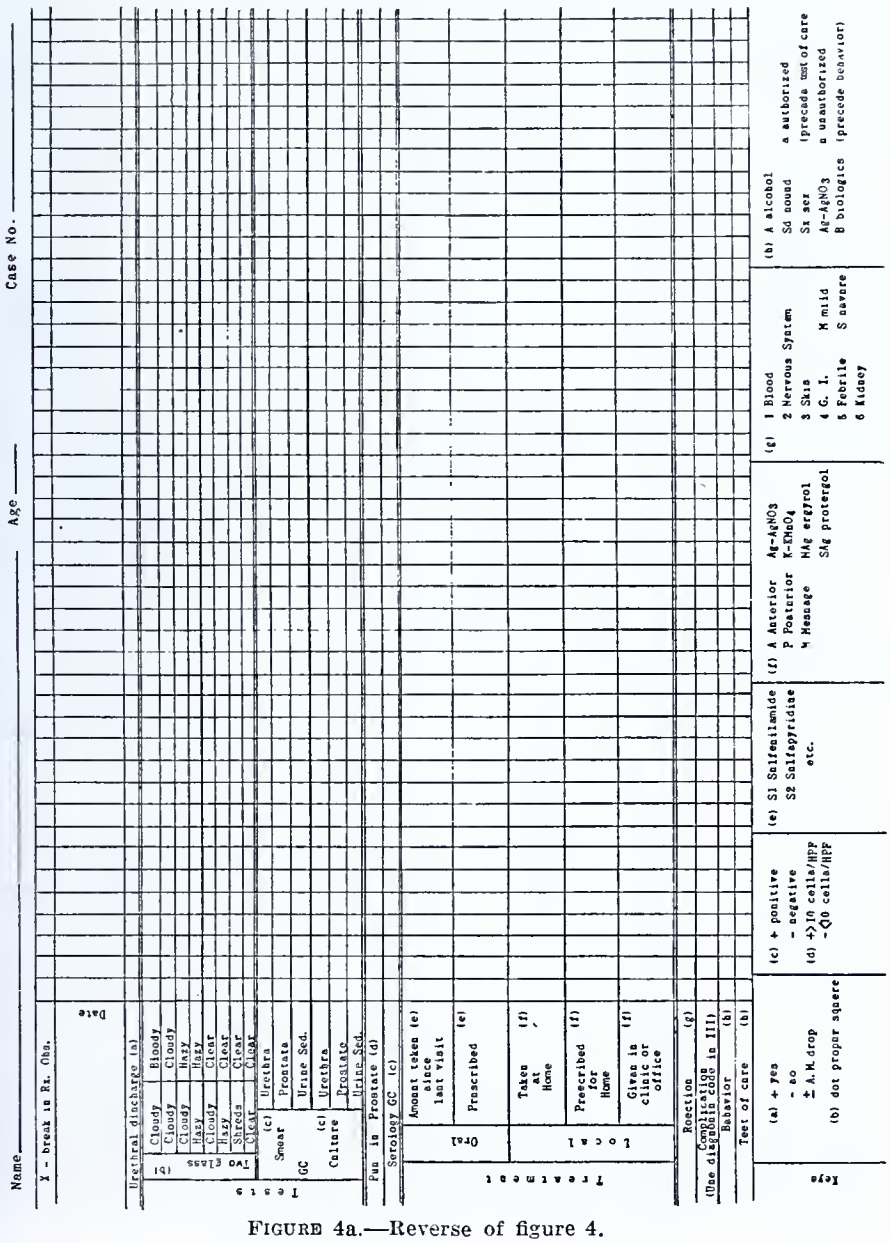


FIGURE 4a.—Reverse of figure 4.

I. IDENTIFICATION

Case No. _____

Admission Date _____ Treatment source _____

Name or Identification _____ Birth Year _____

Address _____

Race: White ☐ Negro ☐ Other ☐ Marital status: Single ☐ Married ☐ Separated ☐ Widowed ☐ Divorced ☐ Work: Light ☐ Average ☐ Heavy ☐

II. MENSTRUAL AND MARITAL HISTORY

Menstrual history: Interval _____ Duration _____ L.M.P. _____

Contraception employed regularly. Yes ☐ No ☐

Dates and duration of all marriages _____

Present Pregnancy: No ☐ Yes ☐ Duration _____ wks

Outcomes All previous pregnancies

	Dates	Abortion (-28 wks)	Premature (29-35 wks)	Labor (36 wks)
1				
2				
3.				
4.				
5.				

III. PREVIOUS GONORRHEA

No ☐ Yes ☐ Dates (first and subsequent attacks) _____

Diagnoses (Specify using code) _____

IV. PRESENT GONORRHEA. ADMISSION

History of Contacts

	Name	Address	Dates exposed	Relationship	Age	Sex	Examination Result	Record No.
1.								
2.								
3.								
4.								

ADMISSION PHYSICAL EXAMINATION

present infection (check normal or abnormal)

	Normal	Abnormal
Urethra	☐	☐
Skene's glands	☐	☐
Bartholin's glands	☐	☐
Cervix	☐	☐
Uterus	☐	☐
Rt. adnexa	☐	☐
Lt. adnexa	☐	☐
Pelvic peritoneum	☐	☐
Rectum	☐	☐
Joints	☐	☐
Lymphatic glands	☐	☐
Heart	☐	☐
Lungs	☐	☐
Kidneys	☐	☐
Other (specify)	☐	☐

Blood count _____

Dates exposed _____ Date appearance

1st symptom _____ Duration symptoms _____ days

Previous treatment present infection Yes ☐ No ☐

Description _____

Diagnosis:

Code

10 Urethritis or skenitis ☐
20 Bartholinitis ☐
30 Cervicitis ☐
40 P.I.D. ☐
50 Proctitis ☐
60 Arthritis ☐

SYPHILIS	Tests Positive	Negative
Admission		
Blood	☐	☐
Darkfield	☐	☐
3 mos. after adm.		
Blood	☐	☐

Clinical findings _____

Remarks _____

Patient history and treatment record - Gonorrhea - Female
U.S. Public Health Service - Field Study

VM-1031

FIGURE 5.—Patient's history and treatment record—Gonorrhea (female).

V. PRESENT GONORRHEA - TESTS, TREATMENT AND OBSERVATION

Name _____ Adm. age _____ Case No. _____

| | | | Date | | |

THE NEWER CHEMOTHERAPY

OF

VENEREAL DISEASES

A Symposium

Supplement No. 13

TO VENEREAL DISEASE INFORMATION

FEDERAL SECURITY AGENCY

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[Released for publication September 18, 1940]

The Treatment of Gonorrhea with Sulfanilamide and Related Drugs: An Analysis of the Cases Treated

HUGH H. YOUNG, M.D., HENRY C. HARRILL, M.D., JAMES H. SEMANS, M.D., and ORMOND S. CULP, M. D., Baltimore, Md.

In the February 1939 issue of *Venereal Disease Information*, some of us presented a survey of the results obtained by the use of sulfanilamide in the treatment of gonorrhea. Since then we have had a much wider experience with the drug and its allied compounds at this clinic, and the literature on the subject has greatly increased. It seems propitious now to assemble the information available and attempt to evaluate these various drugs in the treatment of gonococcus infections in the lower urinary tract.

SULFANILAMIDE

During the 3-year period following the first use of sulfanilamide in the treatment of gonorrhea in this clinic in 1937, we have treated 300 dispensary patients with the drug. Such patients are generally poor cooperators and are the most unfavorable class for treatment and consequently for good results. Of the 300 patients, 93 (31 percent) made only two initial visits to the dispensary and could not be traced further. Consequently no analysis can be made of their cases. But of this number, 40 were free of discharge on the second visit. Ten patients received inadequate amounts of the drug because of their poor cooperation.

There remained then 197 cases for analysis. In 146 of these (74 percent) what may be considered an excellent result with a cure in less than 20 days was obtained. In this group, 102 cases were classified as simple anterior urethritis and 24 as anterior and posterior urethritis, as indicated by the 2-glass test. In these cases the discharge disappeared after an average of 5 days, although in 12 cases discharge persisted as long as 16 days. An additional 27 cases (14 percent) required longer than 20 days to effect a cure. In 4 of these cases, the discharge persisted for more than 30 days. Of this group, 16 were classified as anterior, and 11 as anterior and posterior urethritis. The remaining 24 cases of this group of 197 showed practically no response to the drug and were classified as failures. Only 6 of the 24, however, were regarded as being cases of simple urethritis, and 18 were classified as anterior and posterior urethritis with prostatitis as well when first seen. Moreover, in 12 cases sufficient amounts of the drug could not be administered because of reactions.

We are still convinced of the great value of this drug. A great majority of the patients, at least 80 percent, are able to tolerate the drug with only minimal symptoms. Twenty percent of our patients complained of some symptoms, such as headache, dizziness, anorexia, nausea, vomiting, palpitation, and cyanosis. Usually the severity of these symptoms is in proportion to the amount of drug ingested. Of the 20 percent exhibiting symptoms, only 6 percent presented reactions severe enough to warrant discontinuance of the drug. Among our cases there were no serious reactions. We do not intend to imply that the drug is harmless; we still

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore. This work has been done in cooperation with the United States Public Health Service.

believe that extreme caution should be taken in the administration of the drug, and careful observation of the patients must be undertaken. The value of local injections is still in doubt, although it seems probable that a mild antiseptic solution injected into the anterior urethra in small amounts is helpful. The question of cure should be studied further.

Ten of the patients in this series, while entirely symptom-free with absolutely no discharge, were found to have positive cultures obtained by swabbing the anterior urethra. Were it not for the fact that cultures were taken, these patients would have been considered cured.

We are still of the opinion that a large initial dose, 80 to 100 grains, approximating 0.08 to 0.1 of a gram per kilo of body weight followed by increasing doses over a period of at least 3 weeks, is the most satisfactory method of treatment.

Seven percent of our patients were apparently cured with small amounts of sulfanilamide, totaling no more than 200 grains. These patients made only one or two initial visits to the dispensary and returned from 3 to 6 months later. They said that they appeared to be well after taking the drug for 3 days, that they had discontinued the drug and did not think it was necessary to return for further treatment. On careful examination these patients were found to be well. It is believed, however, that the majority of patients have a recurrence if the drug is stopped after such small doses and as soon as the discharge has disappeared.

SULFAPYRIDINE

An interesting series of cases are those that were unsuccessfully treated with sulfanilamide and then put on sulfapyridine. Among these there were a number of cases that presented serious complications such as strictures, periurethral abscess, urinary fistula, prostatitis, vesiculitis, and epididymitis.

There are 16 cases in this series. The treatment with sulfanilamide which these patients received was considered adequate in every instance. The dosage amounted to 80 grains a day for 2 or 3 days and after that 40 grains a day. The discharge was reduced but never disappeared and gonococci were still present in slide smears or cultures or both. After blood determinations showed the absence of sulfanilamide for at least 2 days, sulfapyridine was started. On each visit a urethral smear, culture, and blood for sulfapyridine concentration, determination, hemoglobin content, and white blood cell counts were taken. Urinalysis for albumin and blood was done from time to time. After the patient had become gonococcus-free and was apparently well, the urethra was massaged over a sound and the prostatic secretion examined before the patient was discharged.

CASE 1. Anterior urethritis; sulfanilamide for 13 days; cultures still positive. Sulfapyridine for 18 days; discharge disappeared and culture was negative within 3 days. The patient was followed 2 months; well.

CASE 2. Anterior urethritis; sulfanilamide for 4 days; cultures positive. Sulfapyridine for 8 days; discharge disappeared in 1 day; 4 smears and cultures negative over a period of 1 month. Patient was seen at the end of 6 months; well.

CASE 3. Anterior and posterior urethritis; sulfanilamide for 8 days; cultures positive. Sulfapyridine for 10 days; discharge disappeared on the second day; cultures negative. The patient was followed for 6 months; well.

CASE 4. Anterior urethritis; sulfanilamide for 14 days; cultures remained positive for 2 months. Sulfapyridine was given for 4 days; discharge disappeared in 1 day; smears and cultures afterwards were negative. The patient was followed 4 months; well.

CASE 5. Subacute gonorrheal urethritis, prostatitis with urethral strictures; sulfanilamide for 15 days; discharge continued with gonococci. Sulfapyridine for 7 days; after 2 days no discharge; cultures negative. The patient was followed 5 months. He was still negative except for chronic prostatitis; no gonococci.

CASE 6. Subacute gonorrheal urethritis and prostatitis; sulfanilamide for 3 weeks; gonococci continued to be present. Sulfapyridine for 6 days; no discharge; cultures and smears were negative after third day. Patient was followed 6 months; well.

CASE 7. Anterior and posterior urethritis; gonococcal septicemia; urethral and blood cultures positive after 10 days of sulfanilamide therapy. Sulfapyridine for 8 days; discharge disappeared; cultures from urethra and blood became negative.

CASE 8. Acute anterior urethritis; sulfanilamide for 10 days; gonococci still present.

ulfapyridine for 10 days; smears and cul-ures negative after the fifth day. The hemo-lobin had fallen to 65 percent during the ulfanilamide therapy but rose to 82 percent 'hile the patient was on sulfapyridine. He 'as followed 4 months; no discharge present.

CASE 9. Anterior and posterior gonorrheal rethritis with old epididymitis; sulfanilamide or 17 days; cultures still positive. Sulfapyri-ine for 14 days; gonococci absent from smears nd cultures after third day. The patient 'as followed 10 weeks; there was no dis-harge and cultures were negative.

CASE 10. Acute urethritis; sulfanilamide or 9 days without a cure. Sulfapyridine for weeks; urethral cultures still positive for onococci. Sulfathiazole then given without esults; cultures still positive.

CASE 11. Acute gonorrheal anterior ure-hritis; sulfanilamide for 9 days without re-ults. Sulfapyridine for 16 days; smears still ositive but gonococci disappeared on the wentieth day. The patient was followed 3 veeks. The cure cannot be definitely attrib-ited to sulfapyridine.

CASE 12. Gonorrheal discharge for 4 nonths; neoprontosil and injections for 6 lays; cultures positive. Sulfapyridine off and n for 1 month due to persistence of prostat-tis, but cultures were negative after the ifth day. The patient was followed 5 months; no gonococci on cultures; some prostatitis.

CASE 13. Acute anterior urethritis. After 13 days of sulfanilamide, cultures were still positive. Sulfapyridine for 11 days; discharge disappeared on third day but cultures were still positive on the eleventh day. Patient was seen a month later; no discharge; cul-tures negative.

CASE 14. Chronic gonorrheal infection, with recent exacerbation, involving prostate, vesicles and epididymes; sulfanilamide for 6 days; cultures were still positive. Sulfapyri-dine given for 31 days; smears and cultures negative after the eighteenth day; old prostat-itis cured by rectal diathermy. Although the patient took sulfapyridine for a month, the hemoglobin remained about 85 percent.

CASE 15. Acute urethritis, prostatitis, semi-nal vesiculitis, old stricture, urinary fistula; sulfanilamide for 20 days; discharge persisted and cultures were positive. Sulfapyridine for 19 days; cultures still positive for gonococci.

CASE 16. Old prostatitis; acute gonorrheal urethritis and epididymitis; sulfanilamide for 2 weeks; gonococci present on cultures at end of 33 days when patient was put on sulfapyridine for 20 days; urethral discharge still present at end of 5 months but then disappeared. The patient was well at the end of a month.

Comment.—A survey of these 16 cases, some of which were complicated by prostatitis, seminal vesiculitis, epididymitis, and stricture, all of which had been unsuccessfully treated with sulfanilamide, show many good results from the use of sulfapyridine.

SULFATHIAZOLE

The latest sulfonamide derivative to be employed at the Brady Institute in the treatment of gonorrhea is 2 (p-aminobenzenesulfonamide)-thiazole, more commonly known as sulfathiazole. This preparation was reported by Fosbinder and Walter in 1939, and to date only 1 case of gonorrhea treated by Pool and Cook with sulfathiazole has been mentioned in the literature. No details are given.

Thirty-eight male patients with gonococcal urethritis have been treated with sulfathiazole at the Brady Urological Institute during the past 3 months. Twenty-one of these have been followed regularly since the drug was discontinued. Seventeen (80.9 percent) have had no recurrence and appear to be cured. Two frank failures and 1 recurrence have been noted. One patient developed anemia and could not tolerate sulfathiazole. Six of the 17 apparent cures were patients with both anterior and posterior urethritis, some of whom had further complicating manifestations of gonorrhea. Two cured patients failed to improve on sulfanilamide. Most of the patients received 1 gram of sulfathiazole every 6 hours. The average duration of treatment was 9.3 days. The discharge disappeared on an average of 2.7 days in cases limited to the anterior urethra and disappeared on an average of 5.2 days in the complicated cases.

Eight male patients appeared to be well but failed to return after sulfathiazole was discontinued. Three of these had posterior involvement. In one case the patient had a mild leukopenia but had no evidence of infection when last seen. The dosage and duration of treatment for this group averaged about the same as in the well-followed cases. Urethral discharge disappeared on an average of 2.8 days and all patients were free from gonococci when last seen.

Nine male patients have had a disappearance of the discharge and negative

urethral cultures but are still taking the drug. Six of these had posterior involvement and in 3 the infection was limited to the anterior urethra. In the latter group the discharge disappeared in 2 days, and in the complicated cases the duration of exudate averaged 4.7 days.

Only 2 instances of toxicity were noted although frequent blood and urine studies were made in each case.

The best results were obtained with those patients who received 1 gram of sulfathiazole every 6 hours until the voided urine was free from shreds. Because of the alleged toxicity of the drug, all patients should be seen at frequent intervals (daily, if possible) and careful examinations of the blood and urine should be made on each visit.

To avoid urolithiasis and leukopenia, we intentionally did not reduce the fluid intake. As a result, the blood level of sulfathiazole only once reached 4 mg. per 100 cc., was generally between 2.5 and 3.5, and in 4 cases reached only 1 mg. percent, although the results were good in all but 4 cases. A higher blood concentration of the drug does not appear necessary in most cases and limitation of fluids should be avoided.

This group is too small to draw sweeping deductions, but after a careful study of the cases we feel justified in saying that sulfathiazole is apparently of great value in the treatment of acute gonorrhea (posterior and anterior) and compares favorably with other sulfonamide derivatives.

REACTIONS

Mild reactions follow sulfanilamide, sulfapyridine, and sulfathiazole—nausea, vomiting, headaches, dizziness, malaise—but these reactions are distinctly less pronounced with sulfathiazole. With sulfapyridine, nausea and abdominal pain are more conspicuous than with the other two drugs. Fever occurs occasionally with all three drugs. With sulfapyridine, conjunctivitis has been reported which is occasionally so severe as to require cessation of the use of the drug. Administration of sulfapyridine and of sulfathiazole is not infrequently associated wit the formation of crystals in the tubule of the kidney and in the urinary tract, a times sufficient to produce hematuria an even to form concretions amounting t small urinary calculi. Pronounced bloo changes occur occasionally with all thes drugs but dangerous agranulocytic ar gina is more common with sulfanilamid than with sulfapyridine and sulfathiazole Cyanosis occurs with sulfanilamide bu not with the other two drugs.

Culver and Herrold report that sulf apyridine is very much more effective i gonorrheal infections than sulfanilamid and that the reactions, with the excep tion of hematuria, are less pronounced.

BACTERIOLOGIC STUDIES

The effect of sulfanilamide, sulfa pyridine, and sulfathiazole on the growth curves of bacteria in urine and pepton has recently been studied by platin methods in our bacteriologic laboratory The action of these drugs on 3 strain of gonococci was tested by incorporatio of the drugs in either chocolate blood o testicular agar (hydrocele plates). I was found that the greatest antibacteria action was obtained with sulfathiazole followed closely by sulfapyridine, bu very little action was observed witl sulfanilamide.

Hill drew the following conclusion from her work: "It is evident from thes experiments that in order of bactericida and bacteriostatic efficacy, these drug may be listed as (1) sulfathiazole, (2 sulfapyridine and (3) sulfanilamide The high concentrations of sulfathiazol which may be obtained in the urine mak it the drug of choice in the treatment o urinary infections. On the other hand the slower elimination of sulfapyridin with the corresponding high blood level make it the drug of choice when th attack is to be made chiefly through th blood stream."

CONCLUSIONS

From the clinical studies made in the wards and out-patient dispensary of th Brady Urological Institute and from the

experimental work in our laboratories, it has been definitely shown that in sulfanilamide, sulfapyridine, and sulfathiazole three drugs of great value in the treatment of gonococcus infections are at hand. These drugs differ in the reactions they produce, as detailed above. The choice of drug used will depend much on the condition of the patient and the reactions produced. As shown in the clinical report, cases that fail to respond to sulfanilamide may sometimes be quickly sterilized by the use of sulfapyridine. Sulfathiazole may also be effective in cases in which the other two drugs have failed. Owing to the less toxic effects of sulfathiazole and its marked bactericidal or bacteriostatic effect in urine, it seems probable that this drug will become the one most highly favored in the treatment of gonorrhea and its complications.

Sulfapyridine in the Treatment of Gonococcal Infections

A Review of 200 Cases

ROLLA R. WOLCOTT, Passed Assistant Surgeon

J. F. MAHONEY, Senior Surgeon

C. J. VAN SLYKE, Passed Assistant Surgeon

Venereal Disease Research Laboratory

U. S. Public Health Service

Staten Island, New York

The advent of sulfanilamide gave increased impetus to the search for new chemotherapeutic agents. One of the newer and better known sulfonamides is sulfapyridine, which has played an important role in combating pneumonia and pneumococcal infections. However, the efficacy of sulfapyridine in the treatment of gonococcal infections has not been so widely publicized, at least in this country.

The following is a brief review of the reports of 10 investigators collected from the literature up to September 15, 1939. Bowie (1938) (*1*) reported apparent cures in an entire series of 30 cases of gonorrhea in men by administering 3.0 gm. of sulfapyridine daily for 4 to 7 days and 1.5 gm. daily for an additional 4 to 7 days. McElligott and Cokkinis (1938) (*2*) in a series of 100 cases obtained 74 percent apparent cures by treatment of "first-week cases"; this number rose to 92 percent in those whose treatment was withheld until the second week. Lloyd, Erskine and Johnson (1938) (*3*) treated 108 cases in men; 33 of the 108 men defaulted. Of those completing the treatment and tests of cure, a satisfactory result was obtained in 68 (90.7 percent). Included in their series were 18 patients whose gonococcal infection had previously failed to respond to sulfanilamide therapy; of these, 17 were apparently cured by sulfapyridine. Prebble (1938) (*4*) reported 12 cures out of 25 cases, using sulfapyridine alone, 25 cures out of 40 when bladder irrigations were added to the regimen. Employing a warm solution of oxycyanide of mercury as a bladder irrigant, as well as oral administration of sulfapyridine, McGregor-Robertson (1938) (*5*) was able to cure 97 of 100 cases; in a second series of 100 cases, in which sulfapyridine was used alone, the cured cases numbered 91. Treating both men and women, Batchelor (1938) (*6*) found sulfapyridine therapy alone to be effective in 92 of 102 cases. Marinkovitch (1939) (*7*) following a rather different schedule of treatment (2.0 gm. daily for 21 days) was successful in 43 of 50 cases (86 percent). Cook and Sutton (1939) (*8*) reported no failures in treating a series

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of 18 patients, 4 of whom were women. At a later date Bowie and his associates (1939) (*9*) effected apparent cures in 118 (92.9 percent) of 127 men treated with sulfapyridine alone; they were unable to demonstrate the value of adjuvant treatment. Durel (1938) (*10*) successfully treated 122 (84.7 percent) of 144 gonococcal infections with sulfapyridine alone.

TABLE 1.—*Summary of 10 reports on sulfapyridine treatment of gonorrhea*

Name	Number of cases	Number of apparent cures	Number of failures	Type of therapy	Sulfapyridine dosage
1. Bowie	30	30	0	Oral + local	3.0 gm. 4–7 days. 1.5 gm. 4–7 days.
2. McElligott and Cokkinis.	100	74% 1st week 92% 2d week	—	Oral	Not mentioned.
3. Lloyd, Erskine, Johnson	108	90.7% 50	7	Oral + local	3.0 gm. 5 days.
		18	0	Oral, parenteral, local	1.5 gm. 5 days.
4. Prebble	25	12	13	Oral	3.0 gm. 5–12 days.
	40	25	15	Oral + local	3.0 gm. 5–12 days.
5. McGregor-Robertson	100	97	3	Oral + local	3.0 gm. 5 days. 2.0 gm. 2 days.
	100	91	9	Oral	3.0 gm. 7 days.
6. Batchelor	102	92	10	Oral	3.0 gm. 5–9 days
7. Marinkovitch	50	43 (86%)	7	Oral	2.0 gm. 21 days.
8. Cook and Sutton	18	18	0	Oral	3 to 4 gm. per day until 5–7 days after negative.
9. Bowie	127	118 (92.9%)	9	Oral	3.0 gm. 4–7 days. 1.5 gm. 4–7 days.
10. Durel	144	122 (84.7%)	22	Oral	3.0 gm. 3 days. 2.0 gm. 3 days. 1.0 gm. 3 days.

MATERIAL STUDIED

In the series studied at the Venereal Disease Research Laboratory of the United States Public Health Service, there were 200 male patients with obvious gonorrheal urethritis. The diagnosis was confirmed by spread and culture methods prior to the initiation of sulfapyridine treatment. For discussion it is well to separate the entire group into two subdivisions: (1) Of the 200 patients, 64 had not received any previous treatment for their infection; (2) 136 had failed to respond to one or more attempted treatments with sulfanilamide.

After the diagnosis was made, the patients were given general hospital care, but they were not confined to bed. In some of the earlier cases the daily fluid intake was restricted to 1,500 cc., but in accordance with laboratory findings this limitation of fluids was later abandoned as nonessential. Sulfapyridine was administered at 4-hour intervals night and day. Frequent urethral spreads and two-glass urine tests were made. Upon complete relief of symptoms, negative findings in spreads and clearing of the two-glass urine test, a urethral sound of moderate size was passed and the penile urethra was massaged. Spread and culture examinations were made of the material so obtained, along with that secured by prostatic massage. These examinations were repeated at least three times.

In addition to the bacteriologic studies blood concentration of sulfapyridine was determined during the course of treatment in 60 patients. Hemoglobin de-

terminations were made in 20 patients and white cell counts in 70. The carbon dioxide combining power of the plasma was studied in 27 cases.

DOSAGE

The usual dosage of sulfapyridine for males of 150 pounds or more in weight was 6.0 gm. per day for 2 days, followed by 3.0 gm. per day for an additional 4 to 6 days. The daily amount was administered in 6 equally divided doses at 4-hour intervals.

The minimum dosage given in 2 days with therapeutic success was 12.0 gm. The maximum amount was 57 gm. over a period of 12 days and this resulted in therapeutic failure. The average total dosage was approximately 28.4 gm. given over a period of 7.3 days.

RESULTS

Apparent cures were obtained in 159 (79.5 percent) of 200 cases of gonorrhea in hospitalized men by the use of sulfapyridine. There was very rapid subsidence of symptoms and disappearance or decrease of the urethral discharge to a slight amount of moisture at the meatus in an average of 2.5 days. Urethral spreads became negative for gonococci in an average of 1.5 days, but it was not uncommon to find occasional extracellular gram-negative diplococci for a few additional days.

Among the 64 previously untreated cases, 56 patients (87.5 percent) were discharged as apparently cured. The duration of infection in these cases ranged from 4 days to possibly 4 years. There were no clinical or bacteriologic

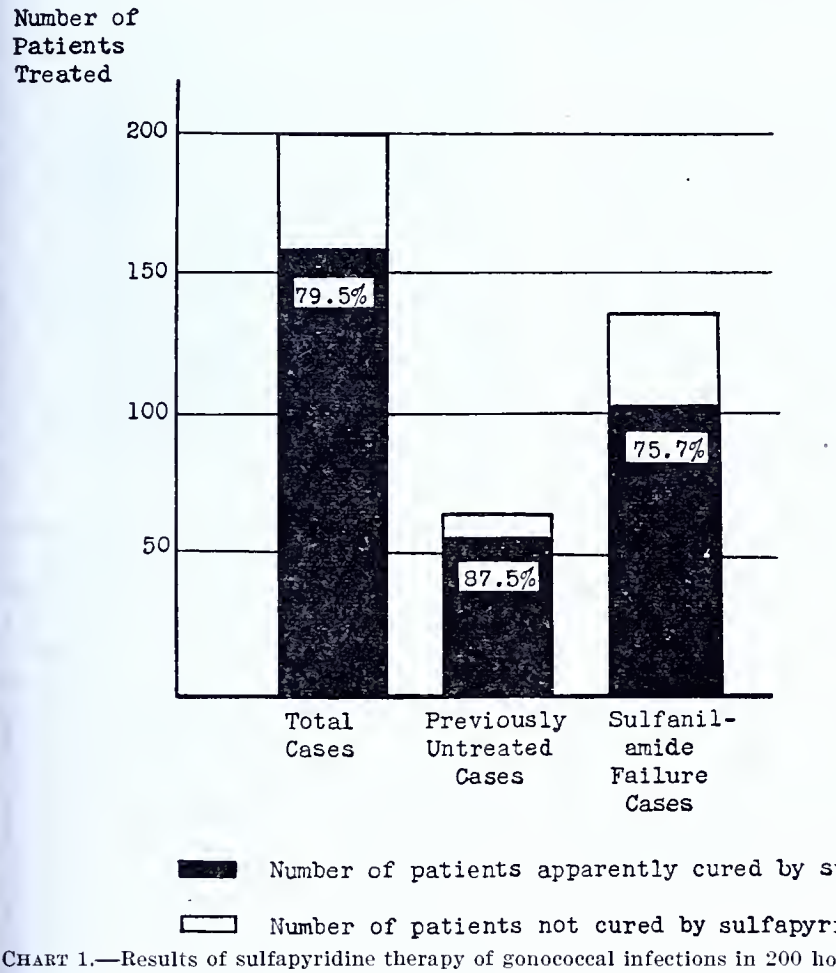

CHART 1.—Results of sulfapyridine therapy of gonococcal infections in 200 hospitalized patients.

indications of any appreciable difference in the therapeutic response to sulfapyridine of acute and chronic gonococcal infections.

Among the 136 patients who had previously failed to respond to one or more attempts at treatment with suitable doses of sulfanilamide, 103 (75.7 percent) were discharged from the hospital as apparently cured. Two to six sessions of induced hyperpyrexia had failed to cure 6 of these patients, and 4 others had not been benefited by the use of sulfanilylsulfanilamide.

There has not been any evidence of a clinical or bacteriologic relapse among those patients who have returned to the hospital for observation.

The 41 patients who were not cured showed an initial response consisting of decrease of discharge and lessening of subjective symptoms. In some the clinical improvement continued although spreads and cultures remained positive. In the others there was a return to the pretreatment clinical status following the early improvement. There was no common clinical factor discernible to which the failures might be attributed. Extension of the disease was not seen while sulfapyridine was being given.

TOXICITY

Toxic reactions to sulfapyridine have been less severe and less frequent than those due to sulfanilamide. Nausea and vomiting were the most troublesome (77 patients had such complaints), but in only a few instances were they sufficiently severe to warrant withdrawal of the drug.

Other toxic responses were as follows:

	Patients
Headache	77
Vertigo	46
Anorexia	26
Weakness	23
Insomnia	20
Skin eruption	11
Cyanosis	7
Nervousness	5
Backache	3
Palpitation	2
Fever	2
Chilliness	1

DISCUSSION

The observations made in this series, together with the conclusions of other investigators, indicate that sulfapyridine is an effective chemotherapeutic agent in the treatment of gonococcal infections, capable of producing a rate of cure comparable to that obtained by the use of sulfanilamide under the most favorable conditions. The compound appears to advantage in the treatment of acute and of ambulatory cases. In comparison with sulfanilamide its lesser toxicity may make it better adapted for general use.

It has been observed that the majority of cases in which sulfanilamide failed have been found extremely resistant to repeated courses of this drug, but 75.7 percent of the 136 patients in the series under discussion did respond to sulfapyridine therapy.

There were no cases of major toxic manifestations such as granulocytopenia, acute hemolytic anemia, hematuria, or peripheral neuritis in the cases studied.

The correlation of blood concentration studies, dosage, and therapeutic effectiveness suggest that it is not necessary to give sulfapyridine oftener than every 6 hours; and that an effective range of blood concentration may readily be reached in the adult with a dose of 3 gm. a day for 2 days, followed by 2 gm. daily for an additional 5 to 7 days.

For these reasons sulfapyridine may, if used with discrimination, prove more valuable in the mass treatment of gonorrhea than its predecessor, sulfanilamide.

SUMMARY AND CONCLUSIONS

Sulfapyridine was used in the treatment of 200 cases of gonorrhea in hospitalized men.

In 64 previously untreated cases sulfapyridine produced 87.5 percent apparent cures, while 75.7 percent success-

ful responses were secured in 136 patients who had previously failed to respond to sulfanilamide in suitable doses.

Sulfapyridine was as efficacious in the treatment of early acute gonorrhea as in the more chronic disease.

It is believed that sulfapyridine may prove very effective in the treatment of this disease.

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THE VALUE OF SULFANILAMIDE IN GONORRHEAL ARTHRITIS

ORMOND S. CULP, M. D. and HUGH H. YOUNG, M. D.
Baltimore, Md.

APPROXIMATELY 2.5 percent of all cases of gonorrhea develop arthritic complaints (*1*). This type of arthritis has run a veritable gamut of therapeutic procedures and, for the most part, the results have been far from satisfactory. Many surgical methods, directed toward the affected joints as well as the primary focus in the genito-urinary tract, have been advocated; a score or more of drugs have been proposed as specific remedies; countless vaccines and serums have been reported with varying results; and almost every known form of physical therapy has been employed at some time. The fact that so many different methods have been tried provides evidence of the inadequacy of most of them. The purpose of this study is to evaluate more simple chemotherapeutic measures which have been employed in recent years at the Johns Hopkins Hospital.

For the sake of simplicity, the cases have been divided arbitrarily into acute, subacute, and chronic groups. All cases of 2 weeks duration or less which presented the usual classical signs and symptoms (pain, tenderness, local heat, redness, swelling, limitation of motion, fever) have been included in the acute group. The subacute cases were of 2 week's to 2 month's duration and were characterized by less severe manifestations of the same symptoms. Those cases of more than 2 month's duration with pain and limitation of motion as the chief symptoms have been relegated to the chronic group.

In evaluating the results of treatment, most writers have been content to group their cases as "cured," "improved," or "unimproved." Although subdividing the degrees of improvement affords opportunity for much criticism, we feel it is essential to do so for the proper appreciation of the changes noted in individual cases. It seems unfair to include patients who were almost entirely asymptomatic with those deriving only slight or moderate improvement from the treatment. For this reason the following degrees of improvement have been employed: (1) *Well*—patients who were entirely asymptomatic on leaving the hospital and who had no joint complaints when seen later in the out-patient department or when treated for some new condition; (2) *marked*—instances in which slight discomfort or limitation of motion persisted; (3) *moderate*—patients who failed to obtain as much improvement in function as the preceding group or who had some degree of recurrence of the same joint complaints after discontinuing active treatment; (4) *slight*—cases with very little but definite improvement in the joint condition; and (5) *none*—patients who showed no appreciable change in symptoms or degree of motion at the end of the course of treatment.

By far the best results at this institution were obtained with sulfanilamide (see table 1).

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore, Md. This work was carried out in cooperation with the United States Public Health Service.

TABLE 1.—*Summary of 22 cases of gonorrheal arthritis treated with sulfanilamide*

Stage of arthritis	Number of cases	Degree of improvement					Cured or markedly improved	
		Well	Marked	Moderate	Slight	None	Number	Percent
Acute	17	10	3	2	2	0	13	76.5
Subacute	4	0	2	0	1	1	2	50.0
Chronic	1	0	0	0	1	0	----	------
Total	22	10	5	2	4	1	15	68.2

Since sulfanilamide was introduced for the treatment of gonococcal infections, hundreds of papers have appeared on various aspects of this type of therapy. In most instances arthritis has been mentioned only incidentally in complicated cases of gonorrhea and only recently has attention been directed primarily toward sulfanilamide in gonorrheal arthritis per se.

Colston, Dees and Harrill (*2*) mentioned 10 cases in which arthritis was present in gonorrhea treated with sulfanilamide. The pains in the joints disappeared on the second day of treatment and the swelling subsided in all cases by the thirteenth day.

Keefer and Spink (*3*) reported using the drug in 3 acute cases and found that 2 of the patients had sterile synovial fluid within 2 days. The other case had a sterile joint effusion before treatment.

Alyea, Daniel and Harris (*4*) mentioned 6 cases of acute arthritis in their discussion of complicated gonorrhea. One patient was left with no arthritic complaints and the others were improved.

Keefer and Rantz (*5*) presented the only comprehensive study of sulfanilamide in the treatment of gonorrheal arthritis. All of their 14 acute cases recovered completely, and the most remarkable results were obtained with cases having infected synovial fluid. These writers found that the optimum effect of the drug was produced only when the blood concentration of sulfanilamide was at least 5 mg. per 100 cc. They also discovered that sulfanilamide diffused into the synovial fluid and was present in approximately the same concentration that existed in the blood. Infected synovial fluid was sterilized within 48 to 72 hours provided the blood concentration was adequate.

Of the 22 patients in our series of arthritis treated with sulfanilamide, 68 percent were cured or markedly improved (table 1). All but 5 of these were acute cases. No complete failures were encountered in this group, and 10 of the 17 acute cases were cured despite the fact that in 2 of them there were bone changes.

CASE 3.—C. G., a colored girl aged 18, admitted July 28, 1938, had a profuse vaginal discharge of unknown duration and arthritis of the right ankle, wrist, and knee for 3 days. Gonococci were numerous in the cervical smear and were isolated on culture from the discharge. The affected joints were swollen, tender, painful, and hot. A roentgenogram of the right ankle revealed some erosion of the bones. Culture from the effusion of the right knee was sterile. A total of 57.6 gm. of sulfanilamide was given orally for a period of 12 days. The blood sulfanilamide concentration reached 9.8 mg. percent. The tenderness disappeared from all joints within 3 days and the swelling subsided completely within 9 days. The patient's hemoglobin dropped from 80 percent to 69 percent but later returned to normal as a result of iron therapy. She left the hospital August 20, entirely asymptomatic and with no vaginal discharge.

CASE 4.—E. T., a colored man aged 38, admitted May 1, 1937, had gonococcal urethritis and arthritis of the left wrist and knee both of 10 days' duration. Gonococci were numerous in the urethral discharge. The wrist and knee were swollen, red, and exquisitely tender. A roentgenogram of the wrist disclosed a small area of destruction in the radius. The complement fixation reaction was strongly positive. The wrist was immobilized with a splint for 4 days. Sulfanilamide was administered orally in daily doses of 5.4 gm. (90 grains) for 6 days. On the third day the blood sulfanilamide concentration reached 7.5 mg. percent and all joint pains disappeared. No urethral discharge could be demonstrated after the fourth day. The patient was discharged on the seventh day, entirely asymptomatic and with no limitation of motion.

The effect of sulfanilamide was less dramatic in 4 subacute cases, but marked

improvement was obtained in 2, slight improvement in 1, and in the fourth case, in which no improvement was noted, the dosage was inadequate.

CASE 18.—C. H., a colored woman aged 23, admitted May 10, 1937, had a profuse vaginal discharge for several years and arthritis of both ankles, knees, and elbows for 3 weeks. No gonococci could be found in the cervical smears or cultures. The joints were swollen, red, painful, and exquisitely tender. Roentgenograms showed no bone changes. The complement fixation test was strongly positive. Culture from the left knee was sterile. No improvement was noted after 3 days of bed rest and sedatives. From May 15 to May 31 the patient was given a total of 48.6 gm. of sulfanilamide. The highest blood concentration of the drug was 5.7 mg. percent on the tenth day. The swelling and tenderness disappeared during the first 7 days and only slight discomfort and limitation of motion persisted at the end of the 16 days of intensive therapy.

Only 1 chronic case was treated and although the blood sulfanilamide concentration reached 9.9 mg. percent, a roentgenogram showed considerable bone destruction and only slight improvement was noted. This obviously was a poor test and affords little opportunity for any clinical deductions. The drug should be tried in more of the subacute and chronic cases before any definite conclusions can be reached.

The dosage and duration of treatment varied markedly, as shown in table 2. The corresponding blood levels also showed great variations and, unfortunately, were not determined in every case. Of the cases not cured, 4 had no blood sulfanilamide determinations. It is quite possible that the levels were not raised adequately in these cases. In most instances the best results were noted when the blood concentration of sulfanilamide reached at least 10 mg. per 100 cc.

In six of the patients anemia developed. One of these required a blood transfusion before leaving the hospital.

The gonorrheal discharge noted on admission disappeared during the period of treatment in each case.

Although most of these patients had cyanosis, anorexia, and general weakness, and the incidence of blood changes was rather high, this type of treatment certainly produced some dramatic results and holds great promise of being the most convenient as well as one of the most efficacious forms of therapy in gonorrheal arthritis. In all probability there will always be some patients who have an idiosyncrasy to sulfanilamide or who fail to respond to the drug in the usual way. A few failures are inevitable.

SUMMARY

Twenty-two cases were treated with sulfanilamide and 68 percent of the patients left the hospital well or markedly improved. Most of the cases were acute and improved amazingly, despite bone changes in two instances. Results were less phenomenal in subacute and chronic cases, but only 5 such patients were studied. Most of the patients had mild toxic symptoms; anemia developed in 6 and 1 required a blood transfusion before discharge. No fatalities resulted.

Chemotherapy appears to be of great value in gonorrheal arthritis. Sulfanilamide is to be recommended for the routine treatment of this condition.

Failures may be encountered due to variations in the individual responses and idiosyncrasies to the drug.

Sulfanilamide should be administered in sufficient doses to maintain a blood level of 10 mg. per 100 cc., if possible. While under treatment, all patients should be followed carefully to avoid severe toxic reactions, and complete blood studies should be made frequently. A drop in the hemoglobin, in the red cell count, and particularly in the leukocyte count should be watched for carefully. Blood transfusions may be necessary.

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TABLE 2.— *Analysis of 22 cases treated with sulfanilamide*

17 ACUTE CASES

Number of case	Race, sex	Age, years	Previous arthritis	Time since onset of last discharge	Organism in discharge on admission	Duration of present arthritis	Joints involved	Previous treatment	Bone changes	Total dosage, gm.	Blood sulfanilamide concentration (mg. percent)	Days treated	Improvement		Remarks
													Arthritis	Urethritis	
1	Negro female	13	Yes	?	Gonococci	5 days	R. knee	Bed rest	Absent	86.4	10.0	16	Well	No discharge, 2 weeks.	Acute symptoms gone in 4 days; swelling disappeared in 14 days; still asymptomatic 1 month later.
2	White female	15	No	?	None	6 days	L. wrist	do	do	105.6	11.1	22	do		No pain after 48 hours, but swelling persisted until eighteenth day.
3	Negro female	18	Yes	1 year	Gonococci	3 days	R. ankle, wrist and knee.	None	Present	57.6	9.8	12	do	No discharge, 10 days.	Tenderness gone in 3 days; swelling disappeared in 9 days; hemoglobin dropped to 69 percent; no leukopenia; asymptomatic 1 month later.
4	Negro male	38	No	10 days	do	10 days	L. wrist and knee.	Bed rest	do	32.4	7.5	6	do	No organisms, 48 hours; no discharge, 4 days.	All joint complaints disappeared after 3 days.
5	Negro female	23	No	2 years	Nonspecific.	5 days	R. wrist; L. shoulder.	do	Absent	48.6	8.3	9	do	No discharge, 7 days.	Pain gone in 24 hours; swelling lasted 7 days; hemolytic anemia; blood transfusion.
6	White female	25	No	2 months	do	2 weeks	R. knee	do	do	19.2	?	8	do	No discharge, 8 days.	No joint pain after second day; swelling disappeared in 6 days.
7	do	23	No	6 weeks	Gonococci	2 days	R. thumb	None	No X-ray.	21.6	2.8	6	do	No organisms, 24 hours; no discharge 3 days.	Pain disappeared in 48 hours; no swelling after fourth day; hot com presses also used.
8	Negro female	9	No	2 years	do	1 day	R. ankle	do	Absent	30.6	?	17	do	No discbarge, 2 weeks.	Acute symptoms relieved in 48 hours; swelling persisted until fourteenth day.
9	Negro male	19	No	1 montb	do	do	R. shoulder	do	do	52.8	6.0	11	do	No organisms, 3 days; no discharge, 10 days.	No pain or tenderness after 3 days; no swelling or limitation of motion after tenth day.
10	Negro female	31	No	?	Nonspecific.	2 weeks	Both elbows, knees, and wrists.	Bed rest	No X-ray.	27.0	10.1	5	do	No discbarge, 5 days.	Asymptomatic on fourth day; mild anemia.

TABLE 2.—*Analysis of 22 cases treated with sulfanilamide*—Continued

Number of case	Race, sex	Age, years	Previous arthritis	Time since onset of last discharge	Organism in discharge on admission	Duration of present arthritis	Joints involved	Previous treatment	Bone changes	Total dosage, gm.	Blood sulfanilamide concentration (mg. percent)	Days treated	Improvement		Remarks
													Arthritis	Urethritis	
11	do	16	No	?	Gonococci	6 days	Both elbows, knees, shoulders, and ankles.	do	Absent	75.6	8.3	14	Marked	No organisms, 1 week; no discharge, 10 days.	Maximal improvement in 7 days, but slight stiffness persisted.
12	do	36	No	?	Nonspecific.	7 days	L. knee	do	do	43.2	11.8	6	do	No discharge, 5 days.	Acute symptoms gone in 48 hours, but slight stiffness persisted.
13	do	13	Yes	?	Gonococci	6 days	R. wrist	do	do	97.2	20.0	18	do	No organisms, 1 week; no discharge, 2 weeks.	Pain and swelling disappeared in 7 days, but slight limitation of motion persisted.
14	do	15	Yes	8 years	do	4 days	L. wrist	None	do	18.0	7.3	5	Moderate.	No organisms, 5 days; no discharge, 6 days.	Pain gone in 48 hours; some swelling persisted; treatment discontinued as hemoglobin dropped to 20 percent; no leukopenia
15	Negro male	58	Yes	38 years	None	1 day	L. knee	do	No X-ray.	24.0	?	10	do		Some pain and swelling continued but hemoglobin dropped to 54 percent; drug stopped; no leukopenia.
16	Negro female	18	No	?	Nonspecific.	5 days	R. wrist	do	Absent	14.4	?	4	Slight	No organisms, but slight discharge persisted.	Hemoglobin dropped to 40 percent after only 4 days of treatment; drug discontinued; no leukopenia.
17	White male	34	Yes	1 month	Gonococci	do	L. knee and ankle; R. wrist and shoulder.	Bed rest	No X-ray.	22.4	?	3	do	No organisms or discharge, 3 days.	Left hospital before treatment was completed.

4 SUBACUTE CASES

18	Negro female	23	No	?	Nonspecific.	3 weeks	Both ankles, knees, elbows.	Bed rest	Absent	48.6	5.7	16	Marked	No organisms, but slight discharge persisted.	Swelling and tenderness disappeared in 7 days but slight limitation of motion persisted.
19	White female	25	No	?	Gonococci	do	R. hip	Heat, east.	do	64.8	11.8	18	do	No organisms, 1 week; no discharge, 10 days.	Asymptomatic after 10 days except for slight limitation of motion which persisted.
20	White male	26	No	2 years	Nonspecific.	6 weeks	Both feet, L. hip and knee.	Vaccine, P. M. I.	No X-ray.	15.4	?	9	Slight	No organisms, 1 week; slight discharge persisted.	Inadequate dosage.
21	do	28	Yes	3 years	None	3 weeks	L. foot, knee, ankle and wrist.	Bed rest, P. M. I.	Present	14.4	5.0	3	None		Inadequate dosage, as well as bone changes.

1 CHRONIC CASE

22	Negro female	47	Yes	8 years	Nonspecific.	5 years	Both wrists, R. ankle, L. knee and hip.	Bed rest	Present	50.4	9.9	14	Slight	No discharge, 2 weeks.	Marked bone destruction.

Venereal Lymphogranuloma. Results following Sulfanilamide Therapy

W. E. GRAHAM, Passed Assistant Surgeon, and E. W. NORRIS, Surgeon, United States Public Health Service

The disease now clinically known as venereal lymphogranuloma is a signal example of how a group of apparently nonrelated, poorly understood pathologic conditions may, in the course of a few years, be shown to have identical etiology and comprise a single disease entity with relatively efficient means of diagnosis. Unfortunately, in medical progress there is often a disproportionate time lag between important scientific discoveries and their clinical application. This is true of venereal lymphogranuloma. Many physicians at the present time have a very vague idea of its real nature and confuse it with granuloma inguinale which is, of course, an entirely separate disease, requiring different methods of diagnosis and treatment.

Frei (*1*) gives an excellent discussion of the development of our present knowledge of the disease, two of the most important landmarks being the proof by Durand, Nicolas and Favre in 1913 that strumous bubo is a separate disease, and the discovery by Frei in 1925 of a specific skin test. The use of the Frei skin test later revealed that esthiomene and inflammatory rectal stricture are, along with strumous bubo and climatic or tropical bubo, manifestations of the same disease. The explanation for the clinical diversity of these manifestations is clearly set forth by Stannus (*2*) who pointed out that in the male the lymphatic drainage from the primary lesion, in nearly all cases, is to the inguinal glands, whereas the drainage from the female genitalia is usually to the perianal and deep pelvic glands, and only when the primary lesion occurs on the urethra, the clitoris, or the anterior portion of the vulva will the inguinal glands ordinarily become involved.

The treatment of venereal lymphogranuloma has been, for the most part, rather unsatisfactory. In attempting to evaluate the results of any particular form of treatment for this disease one must constantly remember that venereal lymphogranuloma has a natural tendency toward spontaneous cure. The long standing ulcerative lesions with draining sinuses which are occasionally seen probably represent exceptionally persistent cases. This contention is supported by surveys which indicate that a comparatively high percentage of those who tend to be sexually promiscuous have been infected. Thus, Haim and Mathewson (*3*) found that of 295 male patients in the U. S. Marine Hospital in San Francisco, 21 percent of those in the venereal disease wards who were tested with Frei antigen reacted positively, whereas only 2.1 percent of other patients had positive reactions to the antigen. Likewise Gray, Hunt, Wheeler and Blache (*4*) in 790 tests done in St. Louis, found that there was a 3.4 percent incidence in the white patients and 40 percent among Negroes. These figures indicate that the disease is much more common than is generally supposed and perhaps in general, more benign. Nevertheless, the disability and death rates caused by venereal lymphogranuloma are sufficiently high to justify more careful investigation of the problem. It is interesting to note that the incidence suggested by the two studies

From United States Public Health Service Venereal Disease Clinic, Hot Springs, Ark.

noted above compares rather strikingly with the incidence of syphilis in comparable groups, if indeed, it is not higher.

OBSERVATIONS MADE AT THE HOT SPRINGS CLINIC

This clinic is unique in that applicants for venereal disease treatments come from every State in the Union. For obvious reasons more come from Arkansas and the adjoining States.

Each year approximately 4,000 applicants are accepted in this clinic for the treatment of one or more of the venereal diseases. Generally speaking one-third of the applicants are colored. During the 2½-year period ending June 15, 1939, 64 (77 percent) of the total of 83 definitely diagnosed cases of venereal lymphogranuloma were among the colored patients. In 3,000 admissions there were 49 (1.6 percent) cases of active venereal lymphogranuloma. On the basis of these figures we may estimate that 3.7 percent of all the colored admissions to the clinic had this disease whereas only 0.5 percent of white admissions were thus infected. No attempt was made to determine the incidence of positive Frei tests among the entire number of clinic patients.

It is quite probable that in the past some cases of venereal lymphogranuloma have passed unrecognized or have been confused with chancroid, granuloma inguinale, or syphilis. The true etiologic factor of many rectal strictures may have been frequently ignored. During the past year, however, a high index of suspicion along with parallel Frei and chancroid intradermal tests in all cases presenting the slightest suggestion of probable venereal lymphogranuloma infection has minimized the number which escaped detection.

TREATMENT WITH SULFANILAMIDE

An attempt was made to evaluate the results of treatment with sulfanilamide. Very satisfactory results had been reported by several other workers, and immediately after the institution of sulfanilamide therapy at this clinic impressive results were obtained. Hamilton (*5*) reported 15 cases. Thirteen of these progressed steadily to complete symptomatic cure and 2 recurred. Shaffer and Arnold (*6*) reported 22 cases. Four of these cases recovered, 11 were markedly improved, 4 disappeared from observation, and 3 were rated as failures. Trautman and Thomason (*7*) reported the treatment of 16 cases with fever therapy and sulfanilamide. They state that the average duration of the disease after treatment was started was 15.3 days.

In August 1938, Shropshear (*8*) reported 9 cases of rectal stricture treated with sulfanilamide. Improvement was noted in each case although no change was seen in the strictures themselves. In February 1939, Knight and David (*9*) reported 2 severe cases of venereal lymphogranuloma, one a rectal stricture and the other a case in which the infection was of the chronic ulcerative type with draining sinuses. Both cases made striking recoveries. Favorable reports are also found in the French and German literature.

To obtain a control group, the records of verified venereal lymphogranuloma cases observed in this clinic since January 1937 were studied. It is realized that this group of cases not treated with sulfanilamide, which is approximately equal to that treated with sulfanilamide, does not furnish a perfect control, but we believe that it does make an interesting comparison which, when properly interpreted, may be significant.

For the purposes of the study, it was decided that the cases of venereal lymphogranuloma could be conveniently separated into three groups. Type I included only those cases in which the primary lesion or simple or suppurating buboes, or both, were present. Type II cases were those which had progressed to a chronic stage (more than 6 months) with ulcerations or fistulas present but without rectal strictures. Patients who had rectal stricture with or without other lesions were all included in type III. Tables 1 and 2 indicate the classification of the entire group of 83 cases by type,

race, sex, and age. The great preponderance of Negro patients should be noted. It is also interesting that the infection was found more often in the 20–29 year age group than in all other age groups combined.

TABLE 1.—*Distribution of venereal lymphogranuloma cases by type, race, and sex*

Type	Male		Female		Total
	White	Colored	White	Colored	
I. Primary lesion and/or bubo, simple or suppurative	14	23	0	1	38
II. Chronic ulcerative type with or without fistulas. No rectal stricture	3	9	0	13	25
III. Rectal stricture, with or without other lesions	0	4	2	14	20
Total	17	36	2	28	83

TABLE 2.—*Distribution of venereal lymphogranuloma cases by age groups*

Age group	Male		Female		Total
	White	Colored	White	Colored	
15–19	0	3	0	1	4
20–29	9	19	2	14	44
30–39	6	9	0	12	27
40–49	2	3	0	1	6
50–59	0	1	0	0	1
60–plus	0	1	0	0	1

A study of the lesions of the disease by age groups did not reveal any noteworthy distribution. The three types were scattered indiscriminately among all ages. The oldest patient, a Negro man of 61, had a primary lesion and inguinal bubo. Nine of the 20 cases of rectal stricture were found in patients in the 20–29 year age group. This distribution is to be expected because the disease commonly progresses from a primary lesion to a rectal stricture within a very few years. One of the patients in this series who had a rectal stricture gave a clear-cut history of onset of the disease only 7 months before admission.

TECHNIC OF TREATMENT

The administration of sulfanilamide was not completely routinized for several reasons. In the first place 47 percent of the entire group of patients also had syphilis, and it was not always considered advisable to give sulfanilamide concurrently with arsenicals, though this was often done when the patient's condition was thought to warrant the slight additional risk of hemopoietic aplasias or of a confusing dermatitis. Unless the lesions were rather acute, sulfanilamide treatment was generally withheld in cases of primary and secondary syphilis until a course of arsphenamine had been administered. Bismuth and sulfanilamide were then given concurrently. Furthermore, an attempt was made to keep the dosage of sulfanilamide near the level of tolerance for an ambulant patient, and this level varied considerably. In general, men received 20 grains 4 times daily for from 2 to 5 days, then 10 or 15 grains 4 times daily for approximately 1 month. Women usually received slightly smaller amounts of sulfanilamide depending upon their weight and their tolerance for the drug. As a rule they received 15 grains 4 times daily at the beginning of treatment; this dose being reduced to 10 grains 4 times daily if the larger dose was not well tolerated. The course was generally terminated at the end of a month, and if more of the drug was considered advisable, it was given after a

rest period of several weeks. Sodium bicarbonate was not given to the patients and they were always instructed not to use "salts". No other relevant treatment was used except routine aspiration of fluctuant buboes, the contents being needed for the preparation of Frei antigen. Most of the patients under treatment were seen daily and all of them were carefully examined at least once each week.

COMPLICATIONS OF TREATMENT

No serious complications of treatment were encountered in the group of 45 patients who received sulfanilamide, although minor reactions such as dizziness, nausea, and slight disorientation were common. One female patient developed a moderately severe anemia after 5 days of treatment. Sulfanilamide was discontinued for 8 weeks. The blood count returned to normal and the patient was then given a smaller dosage for 3 weeks. No complications resulted and there was very striking improvement of the rectal lesions. Another patient who was anemic on admission as a result of rectal hemorrhage was given sulfanilamide and promptly improved, showing increase in weight, return of the blood count to normal, and prompt subsidence of the rectal lesions.

TREATMENT RESULTS IN THIS CLINIC

The results of treatment of venereal lymphogranuloma by old methods and with sulfanilamide in this clinic are indicated in table 3, the cases being classified by types as previously described. It must be remembered that only the immediate results can be considered, as there is no satisfactory way of following up the majority of discharged cases. In evaluating the results of treatment we have tried to classify the cases as accurately as possible into four groups: Unimproved, moderately improved, greatly improved, and apparently cured. Our criteria for the classification of patients in each of these groups is as follows:

1. *Unimproved.*—This group includes all those patients in whom there was no apparent response to treatment. Among this group are two patients who died and several who disappeared from the clinic after only a few days of treatment.

2. *Moderately improved.*—This group includes those who improved under treatment but who left the clinic while they still had open lesions or only slightly improved inguinal or rectal lesions. This group also includes several patients who disappeared from the clinic after only a few days of treatment.

3. *Greatly improved.*—This group includes early cases in which the lesions were almost completely healed but where some induration was still present in the inguinal region. It also includes type III cases where complete subjective relief was obtained, but where rectal strictures were still palpable, and also several type II and type III cases where slight sinus drainage remained.

4. *Apparently cured.*—Only those patients who had no ulcerations, sinuses, or rectal induration or strictures were included in this group. Several of these cases still had slight thickening of the skin at the site of the former inguinal bubo.

Reference to the tables shows that with the former methods of treatment about one-fourth of the total number of cases fell in each of the four result-groups, whereas 77 percent of the cases who were treated with sulfanilamide were considered to be either greatly improved or apparently cured. An objection may be made to the apparent improvement in the results of treatment in those cases in which sulfanilamide is used in that the group of 45 cases so treated was studied with more interest and more intensively than the group of 38 cases treated by the old methods. This objection may be valid, but we believe that it is at least offset by the fact that prior to the beginning of this study some cases of rectal involvement were not recognized as being due to venereal lymphogranuloma. The Frei test was not made in these cases,

hence they are not included in our study. If they had been included, they undoubtedly would have fallen into group 1 or 2 and, therefore, would have made the percentage of good results shown in table 3 lower than are here indicated.

TABLE 3.—*Comparisons of the results of treatment by the old methods*[1] *and by sulfanilamide in venereal lymphogranuloma*

Type	Unimproved		Moderately improved		Greatly improved		Apparently cured		Total	
	Old methods	Sulfanilamide	Old methods	Sulfanilamide	Old methods	Sulfanilamide	Old methods	Sulfanilamide	Old methods	Sulfanilamide
I	3	1	6	0	7	4	6	11	22	16
II	4	0	3	1	1	10	4	2	12	13
III	3	6	1	2	0	6	0	2	4	16
Total	10	7	10	3	8	20	10	15	38	45
Percent	26.3	15.6	26.3	6.7	21.1	44.4	26.3	33.3		

[1] Tartar emetic, fuadin, local applications.

The average treatment-observation periods in the group treated by the old methods and the group treated with sulfanilamide were approximately equal, the average time per person being 68.7 and 66 days, respectively. The average time is somewhat lengthened by the fact that one patient treated by the old methods remained under observation and treatment until her death 26 months after admission, and two patients treated with sulfanilamide were under observation for 14 and 16 months respectively. No other patients were observed for a period longer than 8 months. If these three patients are omitted from consideration, the average treatment-observation time for the two groups is still approximately equal.

The average treatment-time of the eleven cases of simple or suppurating buboes which are entered in the apparently cured column of sulfanilamide treated cases was 20 days. The shortest period was 13 days and the longest 30 days. At the end of this time a few cases still showed slight induration and discoloration of the skin at the site of the bubo. To minimize the danger of recurrence of lesions it is recommended that sulfanilamide therapy be carried out for at least one month, even in those cases in which an apparent cure is obtained in a shorter time.

There are not many reports in the literature regarding the time required for "cure" with various forms of treatment, but the results obtained by other observers are interesting for comparison. Brady (*10*) reports an average hospitalization period of 8 weeks for patients treated with immune transfusions (some of these cases also received other treatment including incision, drainage, and radical excision). Wilmoth (*11*) states that the disease, if treated conservatively, lasts from 2 to 6 months and occasionally longer, and he strongly advises routine early excision of buboes. He states that the wound usually heals by first intention and that in these cases the patient may return to work within 3 weeks. D'Aunoy and von Haam (*12*) also advise adenectomy. They found that in these operative cases healing occurred in 1 month after operation in 50 percent of the cases. Anderson and Harmos (*13*) report 43 cases treated with Frei antigen intradermally. They found that the response to this form of treatment was a gradual reduction in the size of the bubo to a small indurated area within a period of 1 or 2 months.

CASE REPORTS

CASE 1. A Negro man, aged 20, entered the clinic February 8, 1939, for the treatment of suppurating right inguinal adenitis which had been present for 3 weeks. There was a

small ulcer of the coronal sulcus at the frenum, duration 4 weeks. Dark-field examination of the lesion was negative. Kolmer and Kahn tests negative. Frei test was performed but patient failed to return at the time specified for reading of the reaction. In the meantime he had been treating the penile lesion with potassium permanganate soaks with no evidence of improvement. He returned February 13 at which time the Frei test was interpreted as being strongly positive. Sulfanilamide therapy was instituted, 20 grains 4 times daily. In 10 days the penile lesion was entirely healed and the inguinal buboes were rapidly subsiding. By March 8, 1939, the adenitis had completely subsided and there was no evidence of pathologic change except an area of increased pigmentation and slight induration of the skin in the right inguinal region.

Case 2. A white man, aged 29, was admitted to the clinic February 10, 1939, for the treatment of destructive lesions of the penis and bilateral inguinal adenitis. He gave a history of having had a primary lesion in 1934 which was diagnosed as syphilis because of a positive Wassermann test. He stated that he had received, during the ensuing 4 years, 30 injections of neoarsphenamine and 60 of bismuth. The present penile lesions first appeared January 1, 1939, and he had been given 4 injections of neoarsphenamine and 1 of bismuth with no improvement of the lesions. In fact, they had become progressively worse. The Kahn and Kolmer tests were negative at this clinic. The Frei test was positive, and treatment with sulfanilamide was instituted February 12. Improvement in the lesions followed promptly, and they were entirely healed by February 28, 1939. There was slight residual induration of the lymph glands of both inguinal regions when the patient was discharged at his own request February 28, 1939.

Case 3. A Negro man, aged 37, was admitted to the clinic May 18, 1939, for the treatment of bilateral suppurating inguinal adenitis. The glands of the left groin had ruptured spontaneously and there was a profuse seropurulent discharge. The Frei test was reported positive May 19, and sulfanilamide therapy was instituted. The discharge promptly subsided, and the sinuses healed rapidly. There was no evidence of activity by June 8, 1939.

Case 4. A Negro woman, aged 32, was admitted to the clinic December 27, 1938, with seropositive late latent syphilis. Her chief complaints were general weakness, diarrhea, and "hemorrhoids". She gave a history of having had a vulvar lesion which healed without treatment in 1926. She stated that a Wassermann test was reported positive in November 1938 and that she had received 3 injections of neoarsphenamine and 2 of bismuth prior to her admission to this clinic. Her entrance examination showed that she was anemic, markedly undernourished, with moderate distention of the abdomen and multiple perianal skin tags and erosions. Digital examination disclosed marked induration and tenderness of the left half of the rectal wall. There was no definite stricture. The Frei test was positive and sulfanilamide therapy was instituted. There was prompt improvement in her general condition; she gained strength, and the diarrhea subsided within a few days. By January 26 there were no complaints referable to the gastro-intestinal system, the tender induration of the rectal wall had disappeared and all perianal lesions had healed. During this time she had also received 6 intramuscular injections of bismuth. She was discharged at her own request February 2, 1939, and has not been seen since that time.

Case 5. A Negro man, aged 50, was admitted to the clinic October 15, 1938, complaining of ulcerating lesions of the ventral surface of the shaft of the penis and the penoscrotal junction. There was also bilateral inguinal adenitis. The Kolmer and Kahn tests were negative, the Frei test strongly positive. The patient had been previously treated with fuadin and tartar emetic by a private physician. Sulfanilamide therapy was instituted October 21 followed by prompt improvement in the appearance of the lesions. By November 4, 1938, the lesions were almost entirely healed, and the patient requested his discharge.

Case 6. A Negro woman, aged 34, was admitted to the clinic March 14, 1939, complaining of nausea and vomiting, stomach trouble, chronic constipation, and loss of weight. Examination revealed marked malnutrition and abdominal distention with generalized tenderness on moderate pressure. There was scarring and induration of the labia with multiple polypoid growths about the anus. Rectal examination disclosed three distinct strictures through which it was difficult to pass the index finger. The rectal mucosa bled freely following examination. The Kolmer and Kahn tests were negative, Frei test positive. Because of her extreme weakness the patient was hospitalized and sulfanilamide therapy instituted. She received 15 grains of sulfanilamide 4 times daily. Prompt symptomatic relief followed and in one week the abdominal distention had disappeared, and the patient was able to defecate with comparative ease. At the time of her discharge from the hospital April 10, 1939, she had gained 20 pounds in weight and was free from all symptoms. The induration of the rectal wall had entirely disappeared except for one fibrous band representing the proximal stricture, and this was considerably more relaxed than at the time of the first examination. This patient was expected to continue treatment in the out-patient department but left without permission immediately following her discharge from the hospital.

CASE 7. A Negro woman, aged 27, was admitted to the clinic June 2, 1938, complaining of a persistent watery discharge from the vagina. She gave a history of having been irregularly treated for syphilis between 1932 and 1938, having received 8 injections of neoarsphenamine and 12 of bismuth. The Kolmer and Kahn tests were positive. Examination disclosed a rectovaginal fistula and painful granulomatous lesions about the anus. Digital examination of the rectum was not performed because of extreme pain. Antisyphilitic therapy was instituted. No noticeable improvement resulted from antisyphilitic treatment, and the perianal lesions were then treated locally. With the exception of improved hygiene, the local treatment seemed to be of no particular value. A Frei test was made July 26, 1938, and gave a positive reaction. Sulfanilamide therapy was instituted and was followed by rather prompt improvement. The perianal lesions healed completely, and digital examination now disclosed a rectal stricture which would admit the index finger. At the time of her discharge December 21, 1938, the patient was entirely asymptomatic and had gained several pounds in weight. The rectovaginal fistula had ceased discharging early in her treatment, and no attempt was made to repair this surgically. Antisyphilitic treatment was continued throughout her stay at the clinic.

COMMENT

It is conceded that our series of patients who were treated with sulfanilamide is relatively small and not well controlled. Nevertheless, on the basis of previous results in this clinic and the published reports of other observers using other methods, we believe that we have obtained very encouraging results as shown in the examples presented. The tables do not indicate the immediate striking improvement which was witnessed in many of those cases which had not responded to other forms of treatment and in some of which the lesions had been present for years. The natural course of the disease is not entirely clear at the present time. It is not known just how many cases of venereal lymphogranuloma will subside spontaneously and how soon. It is suspected that this percentage is greater than is popularly assumed. We are convinced, however, that radical methods of treatment such as excision of buboes is usually entirely unwarranted. Our patients who had no lesions other than buboes were ambulant and most of them were working during their entire course of treatment which averaged less than 4 weeks. Several of these "apparently cured" cases may have had a relapse later. If so, they have not yet returned to the clinic. But as Hamilton (*5*) reported, such relapses do occur. Surgical treatment of rectal strictures is, of course, sometimes advisable and necessary.

One of the most interesting and striking things observed in our study was the fact that half of the patients who had rectal involvement exhibited marked improvement. Our observations were entirely consistent with those of Knight and David (*9*) and Shropshear (*8*). Two of our more spectacular cases had definite strictures of the rectum before treatment was begun. One of these strictures was so tight that only the finger tip could be inserted. In the other case the finger could be passed with some difficulty. In both cases the stricture completely subsided under treatment. No dilation was used except a weekly examination with the index finger. It seems likely that these two strictures must have been on an inflammatory basis rather than being due to fibrotic changes.

We wish to emphasize that a positive Frei test plus a genital or anorectal lesion does not necessarily prove the presence of active venereal lymphogranuloma. On several occasions, when no improvement was obtained with sulfanilamide or when there was only slight improvement, sulfanilamide was discontinued and tartar emetic therapy substituted with more satisfactory results. In these cases there was probably a mixed infection present, namely venereal lymphogranuloma and granuloma inguinale, only the latter infection may have been active, the former infection having occurred and healed some time previously. We did not observe any beneficial effects when granuloma inguinale was treated with sulfanilamide.

It is hoped that a sufficient number of properly controlled cases will be reported from a clinic where satisfactory follow-up

work is possible so that a true evaluation of the results of sulfanilamide therapy in this disease may be obtained.

SUMMARY AND CONCLUSIONS

1. Venereal lymphogranuloma is briefly discussed, with especial reference to the results obtained with various methods of treatment.

2. Some observations made at the U. S. Public Health Service Venereal Disease Clinic are described.

3. We are convinced that surgical procedures in venereal lymphogranuloma should be limited almost entirely to simple aspiration of fluctuant buboes and to the relief of rectal strictures.

4. We have obtained very encouraging results in the treatment of all types of venereal lymphogranuloma with sulfanilamide, the length of time required for complete subsidence of inguinal buboes being an average of 3 weeks. Eight of 16 cases with rectal involvement were either greatly improved or apparently cured.

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The Treatment of Venereal Lymphogranuloma With Sulfanilamide

ARTHUR W. GRACE, M. D.
and
FLORENCE H. SUSKIND, M. S.
New York

The history of venereal lymphogranuloma in all its varied clinical manifestations is replete with suggestions as to therapy. The fact remains, however, that to date, no completely satisfactory, specific treatment has been evolved.

A study of the disease was commenced at the New York Hospital in 1932. Since that time 229 cases have been seen, practically all of which have been treated by one or more of the methods listed below. Prior to July 1938, these consisted of injections of Frei antigen or antimony compounds; aspiration, excision or incision and drainage of buboes; performance of colostomy with or without resection of the rectum; dilatation of rectal strictures; topical application of balsam of Peru to areas of ulceration on the external genitalia or anorectal region; roentgen-rays to the groin or rectum; medicated enemas; and supportive measures including iron for secondary anemia, salicylates and heat for arthralgia and myalgia, diet and rest.

It was felt that none of these procedures afforded ideal treatment. The most satisfactory results followed the administration of Frei antigen by the subcutaneous or intravenous routes, but only a small proportion of the cases treated in this manner responded well.

At the end of 1938 Gjuric (*1*) reported on the use of a combination of fuadin and prontosil album in the treatment of 23 cases of venereal lymphogranuloma of the inguinal type with good results. He also advised (*2*) 10 percent prontosil album in lanolin salve for application to broken down buboes. Krijnen (*3*) later corroborated this study. At the same time Hamilton (*4*) found that of 15 patients given sulfanilamide alone according to the dosage recommended by Dees and Colston (*5*), all responded with a prompt decrease in the size of the glands. Shropshear (*6*) and Shaffer and Arnold (*7*) showed that the anorectal and genito-anorectal cases did unusually well following administration of the drug. Trautman and Thomason (*8*) and Knight and David (*9*) also obtained very encouraging results with this type of therapy. Peryassu (*10*) employed sulfanilamide alone and in conjunction with roentgen rays, iodine, and antimony. He felt that sulfanilamide alone was to be preferred early in the disease and that it should be combined with roentgen therapy for fluctuant nodes and with iodine or antimony when fistulas existed.

The purpose of this paper is to present the results obtained following the administration of sulfanilamide to 33 cases showing various clinical manifestations of venereal lymphogranuloma. The investigation was begun in July 1938 and carried on to date for a 20-month period.

CASE MATERIAL

Table 1 presents an analysis of the total number of cases of venereal lymphogranuloma seen at the New York Hospital since 1932, and table 2 summarizes the types of cases treated with sulfanilamide.

It is felt that a clinical description of venereal lymphogranuloma and the criteria of classification of the various types of the disease are unnecessary here since this information may be readily found in the literature.

From the New York Hospital and Department of Medicine, Cornell University Medical College, New York, N. Y. This study was aided by a grant from the United States Public Health Service.

TABLE 1.—*Race, sex, and type of disease in 229 cases of venereal lymphogranuloma seen at New York Hospital from 1932 to 1940*

Race and sex	Type of disease					
	Inguinal	Anorectal or genito-anorectal	Genital	Pelvic	Extra-genital	Latent asympto-matic
White:						
Male	45	66	0	0	1	2
Female	2	20	0	1	0	0
Negro:						
Male	12	6	2	0	0	0
Female	2	52	5	0	0	0
Miscellaneous: [1]						
Male	3	5	0	0	0	0
Female	1	4	0	0	0	0
Total white	47	86	0	1	1	2
Total colored	14	58	7	0	0	0
Total miscellaneous [1]	4	9	0	0	0	0
Total male	60	77	2	0	1	2
Total female	5	76	5	1	0	0
Total	65	153	7	1	1	2

[1] Includes Puerto Rican, Mexican, and American Indian.

TABLE 2.—*Race, sex, and type of disease in 33 cases of venereal lymphogranuloma treated with sulfanilamide*

Race and sex	Type of disease	
	Inguinal	Anorectal or genito-anorectal
White:		
Male	2	16
Female	0	3
Negro:		
Male	2	2
Female	1	6
Mexican: Male	0	1
Total white	2	19
Total colored	3	8
Total Mexican	0	1
Total male	4	19
Total female	1	9
Total	5	28

Diagnosis of venereal lymphogranuloma was made on the basis of the clinical picture and the presence of a positive Frei reaction.

In all of the 5 inguinal cases treated with sulfanilamide the involved glands were in the left groin. Four patients presented glands which were fluctuant; in two, sinus formation already had occurred. The fifth showed a mass of tender, matted glands which were nonfluctuant. This patient had had the disease for 10 days when treatment was commenced, the others from 1 to 9 months.

Of the 28 cases of the anorectal type, all had an acute proctitis when sulfanilamide therapy was instituted. Proctoscopic examination of each of the patients revealed the mucosa of the lower bowel to be edematous, ulcerated, granular and friable, and pus and blood could be seen within the anorectal canal. Rectal strictures were present in 20 cases, fistulas in 4, perianal or perirectal abscesses in 2, and concomitant inguinal adenitis in 3. Colostomy has been performed on 2 patients; one was operated on 1 month and the other 1 year and 3 months previously.

The most frequent complaints included discharge of pus and blood from the anus associated with varying degrees of tenesmus and urgent and frequent desire to defecate. Marked constipation was constantly found in the presence of narrow rectal lumina. There were a few cases of abdominal cramps and pain resulting from indolent anal fissures, fistulas or abscesses. Many of the patients complained of constitutional symptoms including lassitude, anorexia, loss of weight, nervousness, insomnia, occasional

recurrent moderate elevations in temperature, and joint and muscle pains.

Uncommon complications of anorectal disease were present in three white men. In one patient a granulomatous growth of the scrotum which histologically resembled venereal lymphogranuloma had developed 4 months earlier; it was removed surgically. Another had a chronic draining sinus from an abscess in the left lower quadrant of the abdominal wall which had been present for over a year. In the third patient, elephantiasis of the penis, scrotum, and right lower extremity had arisen subsequent to extirpation, 4 years previously, of enlarged inguinal glands which accompanied the onset of his rectal condition.

The disease had been present in the majority of the anorectal cases for from 2 to 5 years. In one instance the duration was only 5 weeks and in another as long as 35 years.

METHOD OF TREATMENT WITH SULFANILAMIDE

Ambulant patients received sulfanilamide orally, usually commencing with 0.3 to 0.6 gm. three times a day which was later increased to 0.9 to 1.2 gm. three times a day. The exact dosage depended on the individual tolerance of the patient. Rest periods of 1 to 2 weeks were given on an average at 6-week intervals. In several instances, however, it was found necessary to discontinue the drug for a short time following 1 to 3 weeks' administration, while other patients were able to take sulfanilamide continuously for 12 to 24 weeks without ill effects. When changes in the blood picture occurred, the duration of the rest period was extended. For the inguinal variety of the disease the average length of treatment including rest periods was 4 weeks and for the anorectal type, 29 weeks.

Five of the 33 patients were given sulfanilamide orally during hospitalization. Except when contraindicated by untoward reactions, larger doses were given to hospitalized than to ambulant patients. Usually 7.2 gm. in divided doses was administered on the first day, followed by 5.4 gm. in divided doses on successive days for 6 to 23 days. Two patients, one with inguinal and one with anorectal involvement, did not require further treatment on discharge from the hospital. The three remaining patients, who had the anorectal type of disease, subsequently continued to take the drug as clinic patients.

Progress of the patients was carefully observed by weekly examination and routine proctoscopy. Blood sulfanilamide determinations and complete blood counts were frequently carried out.

Supportive measures such as high calorie, high vitamin, and low residue diets, concentrated vitamin products, and reduced iron were prescribed when indicated.

RESULTS

In table 3 is presented a résumé of the salient facts of each of the 33 cases dealt with and of the results obtained with sulfanilamide therapy.

It is felt that the results presented in table 3 are significant despite the lack of untreated control patients. Although no statistics concerning the natural course of venereal lymphogranuloma are available, the observations of other workers and our own experience over a period of 7 years reveals the disease to be markedly chronic in nature. This is particularly true of the anorectal, genito-anorectal, and genital varieties.

The results obtained with the administration of sulfanilamide will be discussed according to the type of clinical manifestation and the degree of benefit derived, namely, healed, markedly improved, improved, and unimproved.

INGUINAL SERIES

Of the 5 inguinal cases, 4 were completely healed within 3 to 6 weeks after institution of treatment. The fifth patient, who had suppurating glands with sinus formation for 9 months, became free from all signs of disease following 16 weeks' therapy. Three of the 4 ambulant

TABLE 3.—*Résumé of 33 cases of venereal lymphogranuloma and the results obtained with sulfanilamide therapy*

Patient (number)	Age	Sex	Race	Marital status	Type of disease	Additional clinical facts	Duration of disease	Time to improve	Time to effect cure	Duration of treatment	Total amount sulfanilamide (gm.)	Results
1	36	F	N	Married	Inguinal	Si	9 months	3 weeks	16 weeks	16 weeks	82.8	Healed.
2 [1]	36	M	N	Single	do	do	2 months	3 days	4 weeks	13 days	62.1	Do.
3	28	M	N	do	do	fl	3 months	1 week	3 weeks	3 weeks	39.9	Do.
4	39	M	W	Married	do	do	1 month	do	6 weeks	4 weeks	37.8	Do.
5	45	M	W	do	do		10 days	2 weeks	5 weeks	do	37.8	Do.
6	39	M	N	Widower	Anorectal		2 months	3 weeks	39 weeks	39 weeks	330.3	Do.
7 [2]	29	F	W	Separated	do	s	4½ years	18 weeks	79 weeks	76 weeks	278.7	Do.
8	30	M	W	Single	do		2 years	1 week	31 weeks	31 weeks	264.6	Do.
9	42	M	W	do	do		do	8 weeks	24 weeks	24 weeks	245.7	Do.
10	49	M	W	Married	do	s	6 years	3 weeks	19 weeks	25 weeks	220.5	Do.
11	25	F	N	Separated	do	f, g	2 years	1 week	16 weeks	11 weeks	134.1	Do.
12 [1]	38	M	W	Married	do	a, s	5 months	3 weeks	9 weeks	23 days	126.0	Do.
13	43	M	W	Separated	do		2½ years	5 weeks	13 weeks	17 weeks	121.8	Do.
14	42	M	N	Single	do	f, s	2 years, 7 months.	6 weeks	26 weeks	23 weeks	94.5	Do.
15	38	M	W	do	do	s	2 years, 3 months.	4 weeks	9 weeks	7 weeks	44.1	Do.
16	24	M	Mex.	do	do		2 years	9 weeks	23 weeks	32 weeks	34.2	Do.
17	27	F	N	Widow	do	g, s	1½ years	2 weeks		21 weeks	302.4	Markedly improved.
18	32	M	W	Married	do		6 years	10 weeks		24 weeks	297.0	Do.
19	38	F	N	do	do	s	5 years	4 weeks		do	268.8	Do.
20	36	F	W	do	do	do	do	8 weeks		48 weeks	224.1	Do.
21	40	M	W	do	do	f, g	5 weeks	4 weeks		36 weeks	202.0	Do.
22	36	F	N	Single	do	s	2 years	6 weeks		19 weeks	165.6	Do.
23	41	M	W	Married	do	do	4 years	8 weeks		17 weeks	94.2	Do.
24	58	M	W	do	do	a, f, s	1 year	5 weeks		13 weeks	91.8	Do.
25	38	F	W	do	do	s	2 years	3 weeks		10 weeks	72.9	Do.
26 [2]	62	F	N	Widow	do	do	8+ years	2 weeks		66 weeks	64.2	Do.
27	31	F	N	Married	do	do	3 years	3 weeks		6 weeks	56.7	Do.
28 [2]	46	M	W	Single	do	c, s	14½ years	7 weeks		53 weeks	348.0	Improved.
29	55	M	W	do	do	s	35 years	3 weeks		9 weeks	144.0	Do.
30	33	M	W	Separated	do	do	2 years, 8 months.	4 weeks		46 weeks	99.9	Do.
31	35	M	W	Single	do	do	5 years	9 weeks		17 weeks	72.0	Do.
32	36	M	W	Married	do	c, s	3 years			56 weeks	584.1	Unimproved.
33	51	M	W	do	do	s	4 years, 3 months.			62 weeks	266.4	Do.

[1] Treatment during hospitalization.
[2] Treatment during hospitalization and while ambulant.

KEY: a=perianal abscess.
c=colostomy.
f=fistula.
fl=fluctuant.
g=concomitant inguinal adenitis.
s=stricture.
si=sinus formation.

patients required 3 to 4 weeks' treatment with a total dosage of 37.8 to 39.9 gm. of the drug. The hospitalized case was treated for only 13 days during which 62.1 gm. were given.

These figures compare favorably with those of Kornblith (*11*) who found that 83 percent of his inguinal cases treated with intravenous Frei antigen healed in 6 weeks and 12 percent in 3 months.

ANORECTAL SERIES

It must be noted here that fibrous strictures of the rectum were not resolved following administration of sulfanilamide. This fact, however, did not preclude the drug from being a valuable agent in the treatment of venereal lymphogranuloma. Except in the few cases in which the actual fibrotic process caused complete stenosis, tenesmus and constipation were due in considerable part to the acute inflammation and associated edema of the lower bowel. It will be seen in the following discussion, that as long as the anorectal canal remained patent, rectal stricture alone as a residuum of the disease in no way interfered with the well-being of the patient.

Healed cases.—Eleven of the 28 anorectal cases (39 percent) were healed within from 9 to 79 weeks after commencing sulfanilamide. Rectal stricture was present in 5 of these cases. A case was designated as healed when all active lesions in the lower bowel, perianal and perineal regions disappeared including closure of fistulas and fissures as well as resolution of inguinal adenopathy. Symptomatic relief coincided with improvement in the anorectal lesions which began on an average 5 weeks after starting treatment. The passage of mucopurulent and bloody material from the anus gradually diminished and finally ceased altogether; rectal, perianal or abdominal pain subsided; difficulty with bowel movements vanished and a feeling of well-being returned, accompanied by a gain in weight and the disappearance of systemic manifestations including arthralgia and myalgia. The total amount of drug given to any patient varied between 34.2 and 330.3 grams.

Markedly improved cases.—The number of cases showing marked improvement, 11, was the same as the number cured. Strictures were seen in 9 patients. Eight of the 11 patients are still under treatment. Of the other 3, 1 died of an intercurrent lobar pneumonia, and 2 failed to return to the clinic as soon as their condition was alleviated. Improvement was noted on an average 5 weeks after commencing sulfanilamide. The duration of treatment of the group thus far has been from 6 to 66 weeks and the total amount of drug taken between 56.7 and 268.8 grams.

A case was described as markedly improved when examination revealed almost complete healing. The acutely inflamed, ulcerated areas were replaced by granulation tissue and the fissures and fistulas present in 2 cases were disappearing. These patients felt much better generally and were troubled only by infrequent passage of small amounts of discharge from the anus.

Improved cases.—Four patients or 14 percent fell into this classification. All began to benefit by treatment approximately 6 weeks after its inception. A total of 72.0 to 348.0 grams of sulfanilamide was administered over periods of 9 to 53 weeks.

Two persons ceased attending the clinic after improvement began. Of the 2 others one had almost complete stenosis of the rectum with colostomy and the other had partial incontinence of feces following an operation on the rectum. Both of these patients, who are still under treatment, were symptomatically improved and the discharge of pus and blood ceased while taking sulfanilamide. As soon as the drug was discontinued however, the discharge returned but less profusely than formerly.

Unimproved cases.—This group comprised 2 patients. One had had a colostomy for stenosis of the rectum and also had a draining sinus in the left lower quadrant of the abdominal wall; the

ther had a funnel-shaped stricture involving the anal canal as well as destruction of the anal sphincter. The rst patient was given 584.1 grams of ulfanilamide in 56 weeks and the second, 266.4 grams in 62 weeks. There vas no change in the anorectal picture ollowing the use of the drug. In both atients, however, there was a gain in veight, symptoms of toxicity subsided, nd a thinning and slight diminution of he rectal discharge occurred.

ELATIONSHIP BETWEEN CLINICAL MANIFESTATIONS, DURATION OF DISEASE, AND RESPONSE TO THERAPY

In spite of the small number of cases f the inguinal type, it was apparent that his type of venereal lymphogranuloma esponded much more readily to sulfanilmide therapy than did the anorectal ype. A shorter duration of treatment nd a smaller amount of drug was needed o effect healing. The one exception was he case of 9 months' duration which ievertheless required less treatment than lid the majority of the anorectal cases. nasmuch as the inguinal variety of the lisease usually runs a self-limited though rotracted course, the percentages of ures obtained in both series are not trictly comparable.

It was also obvious that in the anorecal series, with the dosage and duration f treatment shown in table 3, there was higher percentage of cures among the ases without than with rectal stricture. Of the 8 cases without stricture, 6 (75 ercent) were healed and 2 (25 percent) vere markedly improved; of the 20 cases vith stricture, 5 (25 percent) were ealed, 9 (45 percent) were markedly imroved, 4 (20 percent) were improved, nd 2 (10 percent) were unimproved.

It is reasonable to consider, however, hat the presence of stricture necessitates onger and more vigorous therapy and hat, with continued treatment, healing nay eventually take place in a much arger proportion of such cases.

As a corollary of the preceding observaion, it was evident that rapid healing was more likely to occur when treatment was initiated early in the disease and before considerable extension of the inflammatory process with concomitant fibrosis and partial occlusion of the lumen of the bowel had taken place.

It must be borne in mind, however, that the intensity of infection may vary in different individuals and occasionally more severe pathologic change may be found in early than in late cases. In table 4 will be found an analysis of the effect of duration of the disease on the response to therapy.

TABLE 4.—*Effect of duration of infection on the response to sulfanilamide therapy*

Duration of disease	Number cases	Results			
		Number healed	Number markedly improved	Number improved	Number unimproved
Less than 6 months	3	2	1	-----	-----
1–2 years	8	5	3	-----	-----
2–3 years	6	2	2	1	1
3–4 years	-----	-----	-----	-----	-----
4–5 years	6	1	3	1	1
6–8 years	3	1	2	-----	-----
14½ years	1	-----	-----	1	-----
35 years	1	-----	-----	1	-----

UNTOWARD REACTIONS TO SULFANILAMIDE

Nineteen of the 33 patients who received sulfanilamide showed some reaction to the drug.

Dizziness, headache, or nausea occurred during the first week of treatment in 6 patients, at the end of the second week in another and after 4 weeks in an eighth person. Two patients complained of shortness of breath and a feeling of oppression in the chest, and 1 of mild attacks of tachycardia after 1 to 3 weeks of therapy. These reactions were readily overcome by a reduction of the dosage, which was sometimes preceded by a short rest period. It was then found possible gradually to increase the dose of the drug without evoking any further untoward reactions.

A change in the blood picture followed prolonged intake of sulfanilamide in 9 patients. A mild secondary anemia developed in 7 persons and 5 showed a moderate depression of the leukocyte count. The institution of a rest period and of iron therapy were sufficient to restore the blood picture to normal when sulfanilamide was resumed.

Table 5 gives an account of the changes in the blood picture which followed sulfanilamide therapy in 9 patients.

TABLE 5.—*Effect of sulfanilamide therapy on blood picture*

Patient (number)	Blood picture			Sulfanilamide therapy	
	Hemoglobin (percent)	Red blood corpuscles (millions)	White blood corpuscles	Total amount of drug (gm.)	Number of weeks continuous therapy
6	95	5.0	4,500	279.9	[1] 23
10	96	3.2	4,500	220.5	25
17	80	4.4	5,000	132.3	8
11	79	3.9	6,500	119.7	9
16	75	3.8	8,000	63.0	5
33	65	3.9	5,000	56.7	7
7	76	3.9	6,500	53.1	5
13	65	3.6	5,000	50.4	5
22	68	3.8	6,500	50.4	5

[1] Including rest periods of 4 weeks and 11 days respectively.

BLOOD SULFANILAMIDE DETERMINATIONS

There seemed to be no definite relationship between the sulfanilamide content of the blood and the ultimate therapeutic effect of the drug. The highest level of total sulfanilamide in the circulating blood occurred in patients who were hospitalized during treatment. It ranged between 8 and 13 mgm. per 100 cc. In only one of the ambulant patients (No. 32), who was listed as unimproved, was the total blood sulfanilamide concentration as high as 10 mgm. per 100 cc.

SUMMARY

1. Since 1932, 229 cases of venereal lymphogranuloma have been studied at the New York Hospital. A number of therapeutic procedures have been employed. The best results were obtained following the use of sulfanilamide.

2. An investigation, carried on over a 20-month period, of the effect of sulfanilamide therapy on 33 cases of the disease is presented. Five cases were of the inguinal and 28 of the anorectal type.

3. Ambulant patients were given the drug in comparatively small doses over a period of 3 to 76 weeks with intermittent rest periods. Hospitalized patients received larger doses of sulfanilamide for 6 to 23 days. The total amount of drug administered to the inguinal cases varied between 37.8 and 82.8 gm. and to the anorectal cases between 34.2 and 584.1 gm.

4. Four of the inguinal cases were healed within 3 to 6 weeks after institution of treatment. The fifth case which was of 9 months' duration was cured after 16 weeks' therapy.

5. Of the anorectal cases, 11 (39 per cent) were completely healed, the same number markedly improved, 4 (14 per cent) improved, and 2 remained unimproved following the administration of sulfanilamide.

6. Fibrous strictures of the rectum were uninfluenced by treatment.

7. There was a higher percentage of cures among the anorectal cases without than with rectal strictures. It is reasonable to consider, however, that the presence of stricture necessitates longer and more vigorous treatment than that given in this study.

8. Rapid healing of the anorectal case was more likely to occur when treatment was initiated early in the disease before extensive pathologic change had taken place.

9. Untoward reactions to sulfanilamide which occurred in 19 patients, were slight and readily controlled.

10. There was no apparent relationship between the total sulfanilamide content of the blood and the ultimate therapeutic effect of the drug.

11. In our opinion, sulfanilamide is a valuable agent in the treatment of venereal lymphogranuloma.

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Sulfanilamide Treatment of Chancroid

ORMOND S. CULP, M. D. and CARL E. BURKLAND, M. D.
Baltimore, Md.

Despite the use of numerous drugs, vaccines, cauterization and various surgical procedures, most cases of chancroid have had a long clinical course and have required most tedious treatment. The purpose of this brief study is to review the literature on sulfanilamide therapy in chancroid infections and to present a series of 25 proven cases of chancroid (with and without bubo) which have been treated successfully with oral sulfanilamide.

LITERATURE

Hanschell (*1*) first reported the use of prontosil in the treatment of chancroid in 1938. He gave an initial dose of 5 cc. of a 5-percent solution subcutaneously, followed by 1 or 2 injections of 10 cc. each at 3-day intervals and simultaneously prescribed oral prontosil album (3 gm. each day in divided doses). All of the 20 patients treated in this manner were cured in from 5 to 10 days. Eight patients also had potassium permanganate compresses applied to the ulcers during sulfanilamide therapy.

One month later Hutchison (*2*) reported 35 cases of bubo, 11 of which were treated with sulfanilamide. Seven of these had typical chancroids and the other 4 patients had old penile scars which were interpreted as healed chancroids. Each was given 1 gram of sulfanilamide every 4 hours and eusol dressings to the penile lesion. The maximum total dosage of sulfanilamide was 13 grams and the minimum was 60 grams. All were cured, the average duration of treatment being 15.5 days. The remaining 24 patients in his series were treated with local heat or intravenous dmelcos vaccine. The period of hospitalization averaged 46 days.

Almost simultaneously, Batchelor and Lees (*3*) published their series of 1 cases of chancroid treated successfully with sulfanilamide. Eight of the patients had complicating bubocs, but all 10 were cured in from 5 to 11 days. The largest total dose of sulfanilamide required was 76 grams and the smallest was 3 grams.

Kornblith, Jacoby and Wishengrad (*4*) reported 45 patients with chancroid who were cured with sulfanilamide alone. The lesions varied in size from 18 mm. in diameter to sloughing of almost the entire glans. The patients received 5.2 grams of sulfanilamide each day for 5 days, followed by half that dosage for 9 more days. All of the lesions were healed at the end of 2 weeks and there were no recurrences during the subsequent 6 months. In a later publication (*5*) the same authors reported 20 additional cases of chancroid which had been cured within 2 weeks by this treatment. Kornblith also tried sulfanilamide powder in several cases as a topical application to the chancroid ulcers and found no variation in the time of recovery.

Fox (*6*) reported a large chancroidal ulcer of long duration which was cured with sulfanilamide. The patient was given 5 grams daily for 5 days and 3 grams each day for the next 28 days.

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore, Md. This study was carried out with the assistance of the United States Public Health Service.

Fields and Weinstein (7) used sulfanilamide powder on chancroids and found that 7 patients were cured in from 7 to 30 days. Most of the patients were well at the end of 16 to 18 days. Topical applications of powdered sulfanilamide were employed 4 times each day after thoroughly cleansing the ulcers.

CASE ANALYSES

During the past 9 months, 25 Negro men with chancroids have been treated with sulfanilamide alone (administered orally) in our out-patient department. All of the patients were cured and no recurrences have been noted. In each instance the diagnosis was made by (a) clinical appearance of the ulcer, (b) negative dark-field examinations, (c) positive dmelcos test, (d) negative Frei test, and (e) the finding of Ducrey bacilli in smears from the lesions.

Eleven of the 25 patients had positive blood Wassermann tests, but as each case was diagnosed latent syphilis by competent syphilologists, treatment for syphilis was not started until the chancroids were healed. The associated syphilis appeared to have no effect on the length of time required for the chancroids to heal.

Five of the patients had gonococcal urethritis when first seen, but during the course of sulfanilamide therapy the urethritis disappeared in each case.

All of the cases have been divided into two groups: (1) Those without associated inguinal adenopathy (12 cases), and (2) those with buboes (13 cases). The time required to cure the patients in the latter group was approximately the same as in the uncomplicated cases.

TABLE 1.—*Chancroid without bubo treated with sulfanilamide; 12 cases in Negro men*

Patient		Ulcers				Previous treatment	Result	Dark field	Frei test	Dmel-eos test	Blood Wasser-mann	Assoei-ated urethritis	Sulfanilamide			Lesion healed (days)
Number	Age	Num-ber	Size	Location	Duration								Total amount	Days treated	Average daily dose	
			Cm.										*Gm.*			
1	18	1	0.5	Glans	2 days	None		−	−	+	−	2 days	42	10	4.2	10
2	29	2	1.0	Glans and prepuee	1 week	do		−	−	+	−	12 days	72	20	3.6	18
3	14	5	.5	do	10 days	Hot eompresses	Unimproved	−	−	+	−	None	37.2	19	2.0	15
4	20	2	.8	Prepuee	2 weeks	do	do	−	−	+	−	do	56	14	4.0	14
5	24	1	3.0	Glans	do	Ointments	do	−	−	+	−	2 weeks	44.8	14	3.2	14
6	18	3	1.0	do	1 week	Hot eompresses	do	−	−	+	−	None	58.8	23	2.5	18
7	23	1	2.0	do	1 month	do	do	−	−	+	+	do	33.6	7	4.8	7
8	51	1	2.0	Prepuee	1 week	None		−	−	+	+	do	27.6	4	6.9	4
9	34	1	2.0	Glans	2 weeks	do		−	−	+	+	do	50.4	14	3.6	10
10	40	1	4.0	do	3 weeks	Hot eompresses (gentian violet)	Unimproved	−	−	+	+	do	64.8	23	2.8	21
11	49	1	3.0	Prepuee	2 weeks	None		−	−	+	+	do	67.2	14	4.8	14
12	58	1	3.0	Glans	10 months	Hot eompresses (powders)	Unimproved	−	−	+	+	do	48	10	4.8	10

Without buboes.—The 12 cases of chancroid without buboes have been summarized in table 1. All of the patients were Negro men, varying in age from 14 years to 58 years. Most of the penile ulcers were of 2 week's duration or less, although one patient had had a typical lesion for 10 months, another for 1 month, and another for 3 weeks before the initial visit to the hospital. In most instances only a single ulcerative lesion was present, but 2 patients had 2 ulcers, another had 3, and one had a total of 5. The lesions varied in size from 0.5 cm. in diameter to massive ulceration of the glans, 4.0 cm. in diameter. Only two of the patients had been circumcised (cases 4 and 11, table 1). Seven patients had tried other types of therapy, chiefly hot compresses and mild antiseptics, without improvement.

Sulfanilamide was started in each case as soon as the diagnosis was established. The dosage was varied considerably despite the fact that no toxic reactions were noted in any of the cases. In each case an equal amount of sodium bicarbonate was prescribed. The best results were obtained with those patients who received an average daily dose of at least 3.6 grams (60 grains) of sulfanilamide. These patients had complete epithelization of the ulcers within 2 weeks. One patient who had a lesion 2 cm. in diameter was cured in 4 days after taking 6.9 grams each day. Another patient with an area of ulceration 4 cm. in diameter required 21 days of treatment before he was cured, but the average daily dose of sulfanilamide was only 2.8 grams. Under intensive treatment, the large ulcers were healed in approximately the same time required for the smaller lesions. None of the cases were called "cured" until the original ulcers were completely epithelized.

The following abstracts illustrate the remarkable results obtained with sulfanilamide therapy:

CASE 1.—A Negro boy, aged 18 years, had had a small ulcer, 0.5 cm. in diameter, on the glans for 2 days and a profuse urethral discharge for the same length of time. No previous treatment had been tried. Smears of the urethral exudate showed numerous gram-negactive intracellular diplococci. Three dark-field examinations of the ulcer on consecutive days showed no Treponemata pallida. The Frei and the Wassermann tests were negative and the dmelcos test was strongly positive. Smears of the penile lesion showed several large bacilli conforming to the morphology of the Ducrey bacillus. The inguinal lymph nodes were not enlarged. For the first 5 days, the patient was given 4.8 grams (80 grains) of sulfanilamide daily in four equally divided doses. Within 24 hours suppuration from the ulcer had ceased and there was evidence of healing. At the end of 3 days the urethral discharge had disappeared and urine cultures revealed no gonococci. The sulfanilamide was reduced to 3.6 grams (60 grains) during the subsequent 5 days with no toxic symptoms. At the end of 10 days the penile ulcer was entirely epithelized and there had been no recurrence of the urethritis. The patient was still well 2 months later.

CASE 7.—A Negro man, aged 23 years, had a dirty ulcerative lesion 2 cm. in diameter on the glans, for 1 month. He had tried various types of hot soaks and compresses, with no improvement. There was no evidence of associated urethritis or glandular involvement. The blood Wassermann reaction was positive. Syphilologists made a diagnosis of latent syphilis. Dark-field examinations of the penile ulcer showed no spirochetes. The dmelcos test was strongly positive and the Frei test was negative. The patient received 4.8 grams (80 grains) of sulfanilamide daily in four equal doses, for 7 days, at the end of which time the chancroid was entirely healed. There was no recurrence during the subsequent 2 months.

CASE 12.—A Negro man, aged 58 years, had had an ulcer 3 cm. in diameter on the glans for 10 months. Numerous kinds of hot soaks, compresses and powders had been tried, with no improvement. The inguinal glands were not enlarged and no urethritis could be demonstrated. The blood Wassermann reaction was positive but was interpreted as indicating latent syphilis. Repeated dark-field examinations of the penile ulcer showed no Treponemata pallida. The dmelcos test was strongly positive and the Frei test negative. The patient was given 4.8 grams (80 grains) of sulfanilamide daily in 4 equal doses, with no toxic reactions, and the lesion was entirely healed in 10 days. There had been no recurrence 3 months later.

In several instances the patients failed to return at frequent intervals as requested and consequently a few continued to take sulfanilamide after the chan-

croids were healed. This explains the variation in a few cases between the "days treated" and "day cured" in table 1. In each case the drug was discontinued as soon as complete epithelization of the ulcers was demonstrated.

From the results obtained in this group of patients, it seems advisable to prescribe an initial dose of 1.2 grams (20 grains) of sulfanilamide 4 times a day, with an equal amount of sodium bicarbonate. If the patient tolerates the drug satisfactorily, more rapid healing will take place if this dosage is continued until epithelization is completed. If any toxic symptoms develop the dosage should be reduced to 10 or 15 grains 4 times a day unless some unfavorable reaction warrants discontinuing the drug entirely. All of the patients in our series of uncomplicated cases tolerated sulfanilamide well; they were cured in an average of 13 days and had no recurrences.

TABLE 2.—*Chancroid with bubo treated with sulfanilamide: 13 cases in Negro men*

Patient		Ulcers				Bubo		Previous treatment	Result	Dark-field	Frei test	Dmelcos test	Blood Wassermann	Associated urothritis	Sulfanilamide			Aspiration of bubo	All lesions healed (days)
Number	Age	Number	Size	Location	Duration	Size	Side								Total amount (gm.)	Days treated	Average daily dose		
			Cm.																
1	22	3	0.5	Prepuce	3 weeks	Large	Left	Hot compresses	Unimproved	—	—	++	—	None	57.6	12	4.8	Yes	10
2	55	1	1.0	Glans	2 months	do	do	Hot compresses, silver nitrate, gentian violet.	do	—	—	++	—	2 weeks	61.2	14	4.4	No	14
3	57	1	2.5	do	18 months	do	Bilateral	Hot compresses, tartar emetic.	do	—	—	+	—	None	48.4	18	2.8	do	18
4	21	1	1.0	Prepuce	7 weeks	do	do	Hot compresses	do	—	—	++	—	do	18	5	3.6	do	5
5	26	2	.5	Glans	1 week	do	Right	Powders	do	—	—	++	—	do	63	21	3.0	Yes	21
6	27	1	.5	Prepuce	4 days	do	Bilateral	None		—	—	++	—	do	43.2	15	2.9	do	15
7	26	2	1.0	Glans	5 weeks	Small	do	Hot compresses	Unimproved	—	—	++	—	do	54	14	3.9	No	14
8	20	2	1.0	do	2 weeks	do	do	None		—	—	++	—	do	48	20	2.4	do	20
9	25	1	2.0	do	4 days	do	do	do		—	—	++	++	do	38.4	8	4.8	do	8
10	36	1	1.5	Prepuce	3 months	do	do	Hot compresses	Unimproved	—	—	++	++	do	54	18	3.0	do	16
11	26	1	4.0	Glans	5 days	Large	Left	Aspiration	do	—	—	++	++	do	72	20	3.6	do	18
12	27	1	2.0	do	4 months	Small	Bilateral	Hot compresses	do	—	—	++	++	2 weeks	58.8	14	4.2	do	14
13	29	1	3.0	do	2 months	do	do	None	do	—	—	+	+	None	81	24	3.3	do	20

With buboes.—The 13 cases of chancroid with buboes have been summarized in table 2. All of the patients were Negro men and ranged in age from 20 to 57 years. Most of the lesions were of several weeks' duration, although a few had been present for only one week or less. The majority of the patients had only a single penile lesion, but 3 had 2 ulcers and 1 had 3 small ulcerated areas. The chancroids varied in size from 0.5 cm. to 4.0 cm. in diameter. Only one patient had been circumcised (case 7, table 2). Nine of the 13 patients had bilateral involvement of the inguinal glands while the other 4 had unilateral buboes. The inguinal lesions in 7 cases were "large" (at least 4 cm. in diameter) while the other 6 were "small" (less than 4 cm. in diameter). In each case the inguinal adenopathy started at approximately the same time that the penile lesion was first noticed. All but four of the patients had tried previous treatment, usually hot compresses and mild antiseptics, but were unimproved. One bubo had been aspirated previously but quickly returned to its former size.

All of the patients were given sulfanilamide orally and an equal amount of sodium bicarbonate as soon as the diagnosis was established. Three of the large buboes became fluctuant and were aspirated. No other supplementary measures were employed in any of the cases. All of the other buboes resolved during the time required to heal the penile ulcers. Treatment was discontinued when there was no further evidence of glandular involvement, and the penile lesions were completely epithelized. In this group of cases, the buboes usually disappeared before the initial chancroid was entirely healed. A few of the patients in this group likewise failed to return at frequent intervals and continued to take sulfanilamide after the lesions were healed, thus explaining the few time variations between "days treated" and "days cured" in table 2. No recurrences were noted in any of the cases.

The daily dosage of sulfanilamid varied considerably but the best resul were obtained with those patients wh received an average of at least 3.6 gram (60 grains) of the drug each day. Unde that regimen, most of the patients wer cured within 2 weeks. One patient wit large, bilateral buboes and a penile ulc 1.0 cm. in diameter was well at the en of 5 days. Three patients required 20 21 days of treatment, but they had re ceived smaller doses of sulfanilamide.

The following abstracts illustrate th phenomenal response to sulfanilamid in these complicated cases:

CASE 1. A Negro man aged 22 years had h 3 small ulcers, each 0.5 cm. in diameter, for weeks on a redundant prepuce. The day aft these were first noticed he began to have so swelling in the left inguinal region, whi gradually increased until, on his initial vi to the hospital, it was the size of a hen's eg Hot compresses had been tried but there h been no improvement. There was a slig suggestion of fluctuation in the bubo. N urethritis could be demonstrated. The blo Wassermann reaction was negative. Dar field examinations of the penile lesions showe no spirochetes. The Frei test was negati and the dmelcos test was strongly positi The patient was given 4.8 grams (80 grain of sulfanilamide each day in 4 equal dos On the third day the bubo was definitely fl tuant and was aspirated without difficul The same dosage of sulfanilamide was cont ued, but the patient failed to return until t twelfth day, at which time the bubo had d appeared and the penile ulcers were heal According to the patient, he had been entir well since the tenth day. No recurrence w noted during the subsequent 4 months.

CASE 4. A Negro man, aged 21 years, h had an ulcer 1 cm. in diameter on a redunda prepuce and a large mass (5 x 4 cm.) in ea inguinal region for 7 weeks. Hot compres had been tried at irregular intervals with o improvement. The blood Wassermann re tion was negative and no urethritis was de onstrated. Dark-field examination of the pen lesion showed no Treponemata pallida. Th buboes were not fluctuant. The Frei test w negative, and the dmelcos test was strong positive. He was given 3.6 grams (60 grain of sulfanilamide each day in 3 equal dos Within 24 hours the suppuration had ceas on the ulcer, and the enlarged inguinal glan seemed to be smaller. At the end of 5 da the penile lesion was entirely healed and th buboes had disappeared. No recurrence w noted up to 2 months later.

Case 12. A Negro man, aged 27 years, had d an ulcer 2 cm. in diameter on the glans d small, bilateral buboes for 4 months. e enlarged glands were approximately 3 2 cm. on each side and not fluctuant. Hot mpresses and hot soaks had been tried, with improvement. For 2 weeks a profuse ethral discharge had been present. Gono- cci were cultured from the urethral exudate. e blood Wassermann reaction was positive, t interpreted as being evidence of latent philis. Dark-field examinations of the penile ion showed no Treponemata pallida. The ei test was negative, and the dmelcos test is strongly positive. The patient was given 3 grams (80 grains) of sulfanilamide each y in 4 equal doses, for 7 days. The chan- oid appeared to be clean within 48 hours. o urethral discharge could be demonstrated ter the fifth day. The inguinal glands re- lved rapidly and were normal on the twelfth y. The penile ulcer was entirely epithelized the fourteenth day. No recurrence was ted during the subsequent 6 months.

From the results obtained with these tients, a daily dosage of 4.8 grams (80 ains) of sulfanilamide should be tried. the patient tolerates the drug well (as d all of these patients) more rapid re- very will be noted if the same dosage is ntinued for at least 1 week. Favorable sults were noted with smaller amounts sulfanilamide, but with these doses nger treatment was usually required. the associated buboes become fluctuant, piration will help to shorten the course therapy. Incision and drainage was necessary in any of these cases. The erage time of complete recovery for e entire group was 14.8 days. No re- rrences were noted.

SUMMARY

Twenty-five patients with chancroids ere treated with oral sulfanilamide one. Of these, 13 had associated buboes hile the other 12 cases were uncompli- ted. All of the patients were cured d no recurrences were noted.

The diagnosis in each case was based the appearance of the ulcer, negative rk-field examinations, negative Frei st, positive dmelcos test, and positive nears from the ulcers.

Patients who received an average of at ast 3.6 grams (60 grains) of sulfanila- mide daily were well within 2 weeks. The period of recovery for the cases with buboes was approximately the same as that for the uncomplicated cases.

In most instances the bubo disappeared before the penile lesion was completely epithelized. Three buboes became fluctu- ant and were aspirated. No other sur- gical measures were employed.

No toxic reactions to sulfanilamide were noted in any of the cases. Five patients had associated gonococcal ure- thritis but this disappeared during the sulfanilamide therapy in each case. Eleven patients had latent syphilis which, however, had no effect on the clinical course of the chancroids.

All patients with chancroid (with or without bubo) should be given 4.8 grams (80 grains) of sulfanilamide each day in divided doses, with an equal amount of sodium bicarbonate. For the optimum therapeutic response this dosage should be continued for at least 1 week, if pos- sible. This may be reduced to 40 or 60 grains each day until the buboes have disappeared entirely and complete epi- thelization of the ulcers has taken place. If it is thought advisable to continue sulf- anilamide longer than 14 days, the dose should be reduced to 40 grains and care- ful blood studies made to discover any drop in red or white cell counts.

Fluctuant buboes should be aspirated but not incised. All patients should be followed carefully at frequent intervals to avoid serious toxic reactions to sulf- anilamide.

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MODERN SEROLOGIC TESTS for SYPHILIS

AND THEIR INTERPRETATION BY THE PHYSICIAN

Josephine Hinrichsen, M. D.

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INTRODUCTION

THE ORIGINAL Wassermann test is so entirely different from some of the highly sensitive and efficient complement fixation tests for syphilis which are in use at the present time, that when the term "Wassermann reaction" is used without a detailed explanation of the mechanism and technic involved in carrying it out, it can only create confusion and misunderstanding. There are now a great many modifications of the original Wassermann test which are known either by the name of the person who has worked out a definite modification or which have been made in one laboratory or another to suit the taste or convenience of the user and to which he refers simply as a "modified Wassermann test."

Unfortunately many of these Wassermann technics still in use and on the basis of which clinical studies are reported, have not been modified to include features which have been demonstrated to give the most sensitive and at the same time the most specific results. Many of them still make use of aqueous tissue-extract or nonsensitized alcoholic-extract antigens as well as of various procedures in the test which have been definitely shown to produce unreliable results; for example, the continued use of incubation at 37° C. instead of ice-box incubation and the procedure of allowing the tests to stand overnight after the addition of cells before reading the results. Yet many of the studies on syphilis reported in the literature are based on these insensitive and unreliable tests, with the result that these studies are also unreliable. The uncritical reader is misled, and the one who is aware of the situation laments the waste of effort in what should be extremely valuable studies if carried out on a sound basis.

There is great need, therefore, of using one, and certainly not more than a few, well-established, efficient complement fixation tests as a control for all comparisons that are made between flocculation and complement fixation tests for the purpose of evaluating these tests and for clinical studies which are of interest to physicians who are not serologists.

The best choice of such a standard complement fixation test at this time is the Kolmer test. There is no other complement fixation reaction which has better stood the test of time or which has been more acclaimed by a large number of competent investigators than the Kolmer test. It is lamentable, therefore, that in practically none of the comparative evaluations of definite flocculation tests, such as the Eagle, the Hinton, the Kahn, the Kline, has the Kolmer test been chosen for comparison, with the exception of those made under the auspices of the Committee on Evaluation of Serodiagnostic Tests in the United States. Nearly always the comparison

is made between the Eagle, Hinton, Kahn, or Kline and "the Wassermann reaction," or "a modified Wassermann reaction" whose technic is usually not described. Consequently, most of these comparative studies are of little or no value. If an inefficient complement fixation test has been used for comparison it gives the particular flocculation test in question an undeserved high rating.

The failure of most investigators to apply a standard complement fixation test to the study of various clinical phases of syphilis as well as to comparative studies between flocculation and complement fixation tests makes much of the literature worthless.

In this study, therefore, no attempt will be made to review completely the literature. Furthermore, the discussion will be limited to the tests which have been most firmly established in the United States and which have been shown to have definite value and are therefore of most interest to the clinician. These tests are the Kolmer complement fixation reaction, the Eagle complement fixation reaction, and four flocculation reactions, namely, in alphabetical order, the Eagle, the Hinton, the Kahn, and the Kline tests.

It is difficult even for experienced serologists to compare the various well-described modifications which have been established with one another on a sufficiently large series of cases to establish their comparative worth as tests. Such an evaluation would require that a large number of competent serologists compare all of these modifications on a sufficiently large group of persons with all types of syphilis, persons without syphilis, and persons with other diseases. No such cooperative study on all the definitely established modifications of the complement fixation reaction has as yet been made.

For this reason, when a physician, especially one who is not a serologist, in going over the literature reads about a certain modification of the Wassermann test as applied to the diagnosis, treatment-results, incidence, or some other phase of syphilis, he will question (if he is at all thoughtful) whether this modification compares favorably in regard to sensitivity and specificity with reliable modifications applied to similar studies of syphilis. Because if it does not, it is of no value, and he is wasting his time reading the article. But unfortunately he often cannot determine the relative value of the particular modification and is therefore also uncertain in regard to the results of the study which are based on such a test.

When the test used is referred to simply as "the Wassermann test" or "a slightly modified Wassermann test," then the most important factor of the whole study is an unknown and can therefore form no basis for evaluation.

This confusion does not exist in connection with the flocculation tests for syphilis. One never reads an article in which the statement is made

that "a flocculation reaction" or "a modified flocculation reaction" was done. The modification is always definitely stated, for example, "The Kahn presumptive test," "the Kahn diagnostic test," "the Hinton test," "the Kline diagnostic test" or "the Kline exclusion test." Since these are well-standardized tests, the reader immediately knows the nature of the test. He knows a great deal more about the comparative value of these different modifications of the flocculation reactions than of those of the complement fixation reaction because, as already pointed out, they are well defined, they are fewer in number, and more comparative studies which are valid have been made. He is definitely puzzled only when the writer, instead of following the exact technic as outlined by the originator of the test, states that he has "slightly modified" the technic. Even if the modification is described, the reader often does not know whether or not this modification has been done at the expense of sensitivity and specificity.

COMPLEMENT FIXATION TESTS FOR SYPHILIS

Before considering the modified complement fixation tests of Kolmer and Eagle, the mechanism of the complement fixation reaction, as outlined by Stokes (*120*), will be presented for the sake of completeness. This reaction is based upon the Bordet-Gengou phenomenon of fixation of complement. Five distinct substances are used which interact in two groups. These groups are called the antigenic and the hemolytic systems. The hemolytic system is an indicator of what has happened in the antigenic system. The five elements entering into the reactions are:

1. Complement, a chemical substance present in normal and pathologic blood in man and animals. It can be destroyed by heating to 56° C., and when thus destroyed the serum is said to be "inactivated" and complement from another source must be added before the complement fixation reaction can be carried out.

2. Syphilitic amboceptor (reagin) a substance which appears in the blood as a result of syphilitic infection and which is not destroyed by heat. This element and the complement form the reacting parts of the syphilitic patient's serum.

3. Syphilitic antigen, extracted from syphilitic and certain other tissues and added to the serum for the purpose of binding the complement through the intermediation of the syphilitic amboceptor (reagin). The union between these two substances is permanent and when quantitatively carried out results in the absolute "fixation" of the complement so that it cannot participate in the subsequent hemolytic indicator reaction.

4. Red blood corpuscles, obtained usually from sheep or man, washed and used quantitatively in a physiologic saline suspension. The lysis of these red blood corpuscles by their union with any unbound complement through the intermediation of the hemolytic amboceptor indicates a "negative" complement fixation reaction.

5. Hemolytic amboceptor, which is obtained by immunizing a laboratory animal, usually a rabbit or dog, against the red blood corpuscles of sheep or man. When these red blood corpuscles are injected into the animal, the animal develops a specific hemolytic amboceptor which, combining with the normal complement of serum, produces hemolysis of the injected red blood corpuscles within the animal's body. This reaction can be transferred to the test tube by using the animal's serum with a supply of the corresponding red blood corpuscles (see 4 above) to serve as an indicator for the presence of unfixed or unbound complement in the complement fixation reaction.

The antigenic system is composed of (*a*) complement, present in the patient's serum, or, if this has been inactivated, added in the form of guinea pig complement, (*b*) syphilitic amboceptor (reagin), also present in the patient's serum if the patient has syphilis, but absent if he does not have syphilis, and (*c*) syphilitic antigen, added to the serum in an amount proportional to the amount of complement known to be present, so that complete fixation will occur if the requisite amount of syphilitic amboceptor (reagin) is present. The mixture of these reagents is subjected to incubation and refrigeration. If syphilitic amboceptor (reagin) is present, the complement is fixed to the antigen and the serum becomes incapable of reacting to the subsequent addition of the hemolytic indicator system. If syphilitic amboceptor (reagin) is not present, the complement remains free and can enter into the next reaction, as soon as the hemolytic amboceptor and red blood corpuscles are added. The second system is, therefore, an indicator of what has happened in the first.

The hemolytic system is composed of (*a*) hemolytic amboceptor in known amount, consisting of the serum of the immunized animal, and (*b*) suspension of red blood corpuscles in an amount to correspond to the complement originally present and to the amount of hemolytic amboceptor added. The mixture of the two systems is again incubated at body temperature.

If the patient has syphilis all of the free complement will have been fixed by combination with his syphilitic amboceptor (reagin) and the added antigen, and none will be available for the hemolysis. If the patient does not have syphilis, all the complement will remain free or unfixed for participation in the hemolytic indicator reaction as soon as the second group of reagents is added, and complete hemolysis of the red blood corpuscles will take place. The degree of hemolysis which occurs is to some extent a measure of the intensity of the Wassermann reaction. The more hemolysis the weaker the reaction. The more accurate method of making quantitative estimations of the degree of positiveness, however, consists in varying the amounts of reagents used, and especially of the fluid or serum which is being tested. Strongly positive serums produce complete inhibition of hemolysis in very small amounts.

Kolmer Complement Fixation Test

Kolmer published his modification of the Wassermann reaction in 1922, following 6 years of intensive investigation of all phases of the test. Except for slight changes in the amount of serum employed, improvement in the sensitivity of the antigen, and the adoption of an improved method for titration of antigen for determining the optimum dose to employ, no important changes in the test have been made from that time to the time of the last publication of the method in 1940. The purpose of Kolmer's studies was to develop a test of maximum specificity and sensitivity. The aim was

to determine an amount of serum or spinal fluid which would be sufficiently large to make possible the detection of the smallest amounts of syphilitic antibody (reagin) without giving nonspecific or anticomplementary reactions. In the Kolmer technic 0.2 cc. of serum and 0.5 cc. of spinal fluid were found satisfactory and equivalent to approximately 0.6 cc. of serum and 3.0 cc. of spinal fluid in terms of the original Wassermann test. The sensitiveness of the test was increased by means of the following factors (*67*): (1) A highly sensitive antigen, (2) the use of large amounts of antigen, (3) the use of relatively large amounts of serum and spinal fluid, (4) heating serums for only 15 minutes at 55° C. instead of for 30 minutes, which results in much less destruction of reagin, (5) using a mixture of guinea pig complement prepared in a manner tending to increase sensitiveness to fixation, (6) mixing serum and antigen for a brief period before the addition of complement in setting up the test, which was found to increase slightly the sensitiveness of the reactions, (7) using a primary incubation of 15 to 18 hours in a refrigerator at 6° to 8° C., (8) close adjustment of the hemolytic system in order to avoid excessive amounts of complement and hemolysin (this is accomplished by titrating both hemolysin and complement before the main tests), (9) using an antisheep (preferably) or antiox hemolytic system, and (10) reading the reactions within 3 hours after the conclusion of the secondary incubation.

The requirements of practical specificity were met by the following:

1. Close adjustment of the hemolytic system to a primary incubation of 15 to 18 hours at 6° to 8° C. in order to supply sufficient complement and hemolysin for nonspecific fixation and yet to detect the slightest degrees of specific fixation by syphilis antibody and antigen.
2. Careful titration of antigen under conditions rendering the dose employed suitable for a primary incubation of 15 to 18 hours at 6° to 8° C.
3. Including controls in every test and especially serum, antigen, and hemolytic controls to detect anticomplementary activities of serum and antigen or defects in the hemolytic system, also corpuscle controls to check the tonicity of the saline solution and the fragility of cells. Tests with serums from healthy, normal, and from syphilitic individuals should be included as positive and negative controls.

The technic of the Kolmer and Eagle complement fixation tests, as well as that of the Eagle, the Hinton, the Kahn, and the Kline flocculation tests has been published (*124, 70, 105*) and therefore will not be given in this paper.

It might be of interest, however, to point out that since Kolmer's latest publication of the technic of his test, Boerner and Lukens (*9*), working in Kolmer's laboratory, have simplified the technic by the mixing of certain of the reagents in bulk. Antigen and complement are combined and are added as a single increment to the patient's serum, and sheep erythrocytes

are sensitized and are measured into the various tubes at one time and not as two different additions. The advantages of this technic are said to be increased accuracy and the saving of time. Boerner, Jones and Lukens (7) have also published a simplified method for the preparation of antigen. This antigen contains 0.4 percent of cholesterol.

Comparison of Kolmer and Eagle Complement Fixation Tests

The chief differences between the Kolmer and the Eagle complement fixation tests are that Eagle makes use of an ice-box incubation period of only 3 to 4 hours as compared to 15 to 18 hours by Kolmer and that Eagle uses 0.6 percent of cholesterol plus 0.6 percent corn germ sterol in his antigen as compared to the use of only 0.2 percent of cholesterol in the Kolmer antigen. Kolmer, Richter and Yagle (*67*) made a study of the sensitization of antigen and found that sensitization of antigens for the Wassermann reaction with cholesterol, sitosterol, and other sterols has an important relation to the kind of primary incubation and amount of complement employed. They found that with a primary incubation period of 15 hours at 6° C., followed by 10 minutes in a water bath at 37° C., antigens sensitized with more than 0.2 percent cholesterol or other sterols tend to yield falsely positive reactions with nonsyphilitic serums in the Kolmer test. Antigens sensitized with 0.4 percent of cholesterol were found to be too sensitive for tests employing this period of primary incubation, although probably acceptable when used with a primary incubation period of 4 hours at 6° C. with or without an additional incubation of one-half hour at 37° C. Antigens sensitized with 0.8 percent of cholesterol and 0.6 percent of sitosterol were found to yield nonspecific falsely positive reactions in the Kolmer method with both kinds of primary incubation.

Kolmer (*62*), in a review of the literature in regard to antigens, points out that the first "antigens" employed by Wassermann, Neisser and Bruck and by Detre were salt-solution extracts of syphilitic tissues, pure cultures of Treponema pallidum not being available. With these extracts the reactions were considered biologically specific. No one supposed that the mechanism was entirely different until Marie and Levaditi, and Landsteiner, Müller and Pötzl showed that similar extracts of nonsyphilitic tissues and alcoholic extracts of guinea-pig heart, served equally well as "antigen" in the Wassermann test. One result of the researches stimulated by this discovery was to show that the real antigenic substances in both salt-solution and alcoholic extracts of either syphilitic or normal tissues were lipoidal bodies. Much work was done on the identification of these. The results showed that many lipoidal substances were concerned, that no one was as good as a mixture, and that synthetic "antigens" were generally unsuccessful. Noguchi's studies, continued by Bronfenbrenner, resulted in the discovery that the phosphatids, particularly lecithins, were highly anti-

genic and in the working out of a method for preparing these from tissues. They are now well known as the extracts of acetone-insoluble lipoids. While numerous researches had shown that alcoholic solutions of cholesterol were but feebly antigenic, Browning, Cruickshank and McKenzie found that the addition of cholesterol to solutions of lecithins greatly improved their antigenic value. Sachs found that the addition of cholesterol to alcoholic extracts of heart muscle greatly improved the antigenic value of such extracts. These discoveries may be said to have ushered in a third epoch in the development of "antigens" for the Wassermann test. These cholesterolized extracts have come into general use and are regarded by many serologists as approaching closest to the ideals of a standard antigen.

Although Kolmer and his associates have found that cholesterolized extracts increase the tendency to nonspecific reactions, Kolmer points out that this can be prevented by technical factors and that cholesterolized alcoholic extracts are probably the best "antigens" for the Wassermann test. Most serologists employ 0.2 to 0.4 percent of cholesterol. They have avoided larger amounts because they believe that these may oversensitize and yield nonspecific reactions. Eagle, however, states that concentrations as high as 0.8 percent still further increase the sensitivity of antigen-lipoids without danger of producing biologically false positive reactions, providing technical error can be excluded. He also found that of 50 substances examined by him, sitosterol, a sterol obtained from the nonsaponifiable fraction of wheat germ, ranked next to cholesterol in sensitizing activity. Later he replaced sitosterol by corn germ sterol.

Since cholesterol is not in itself antigenic, Eagle explains its fortifying effect on the antigen as being due to the fact that it causes a coarsened dispersion of antigen by forming a relatively large nucleus upon which antigen is adsorbed. The larger the antigen particle, the greater is its avidity for reagin per unit surface (*27*).

Serum in concentrations greater than 1:25 causes a marked inhibition of complement fixation in general and of the Wassermann reaction in particular. The serum protein is probably adsorbed by the colloidally dispersed lipoid-reagin complexes, forming a protective film which prevents the fixation of complement. This inhibition explains the zone phenomenon in complement fixation: A weakly positive serum may give a completely positive reaction in 1:5 dilution, for example, and yet, because of this serum inhibition, may appear completely negative when tested as whole serum. The greater sensitivity of the test when ice box incubation is used instead of incubation for one-half hour at 37° C. is due to the fact that this serum inhibition is less marked at lower temperature, to the prolonged incubation time which allows greater specific fixation, to a more marked nonspecific destruction of complement by antigen, and a spontaneous deterioration in the longer ice box test. Because of the inhibition by serum protein in high

concentration, a quantitative Wassermann technic, involving the use of graded quantities of serum, is worthless when carried out at 37° C. Even the ice box test, which is less susceptible to this inhibiting effect, will yield a positive reaction with whole serum only when the circulating reagin exceeds a surprisingly high threshold (6 to 10 times the quantity which could be detected in dilute serum).

The flocculation reactions are relatively unaffected by serum in excess, with the result that serum zone reactions, although they occur, are comparatively infrequent. Spinal fluids, which do not contain the inhibiting agent, never show this type of zone reaction.

Eagle (*27*) is of the opinion that with a highly sensitized antigen, the difference in sensitivity between a 15-to-18-hour ice box test and one of only 4 hours' duration, followed by one-half hour at 37° C. is too small to justify the longer incubation as a routine procedure. He points out that there is more danger of complement deterioration in the 18-hour test and that a highly sensitized antigen cannot be used with the longer incubation because of its anticomplementary properties.

At least five properties of serum affect the results obtained in the Wassermann reaction and should be considered in determining the optimum quantity to be used in a routine test—its reagin content; its anticomplementary activity; the amount of native amboceptor; the amount of native complement; the fact that serum protein, or a substance associated with it, inhibits the fixation of complement by the lipoid-reagin compound.

The serums of syphilitic patients are not either "positive" or "negative" but contain widely varying amounts of the specific substance responsible for their reactivity with tissue extracts. Other things being equal, the more reagin present in a serum the more intense is the reaction with antigen and the more complement is fixed by the resultant antigen-reagin compound in a given time interval. One would suppose therefore that the sensitivity of the test would increase in direct proportion to the amount of serum used. There are certain factors, however, which modify this situation. They are as follows:

1. Anticomplementary activity of serum. A serum is called anticomplementary when it destroys complement under the conditions of the test even without the addition of antigen. Since this fixation occurs in the absence of reagin, it is essential to include a serum control containing serum and complement without antigen in every Wassermann test, to be sure that the serum has no effect on the complement and that the disappearance of complement in the test proper is due to the actual presence of reagin. If this control tube fails to hemolyze, the serum is anticomplementary and such a report has no diagnostic value.

Anticomplementary reaction of serum may be due to bacterial contamination, to the presence of chemicals in the collecting tube, and to technical

factors; it may even occur with fresh, properly collected serum. The incidence of anticomplementary reaction is several times as great in syphilitic serums as in normal serums. In spite of this fact, reports of anticomplementary reaction have no diagnostic significance.

2. Native complement content of serum. The complement content of different serums varies widely. In order to avoid the necessity for the enormous task of accurate titration of the complement activity of each serum to be tested, the great majority of laboratories destroy native complement by incubating the serums at 56° C. for 15 to 30 minutes and then adding a constant quantity of fresh guinea pig serum (complement) to each serum to be tested.

3. Native amboceptor. Fresh serums frequently contain native amboceptor (hemolysin) for sheep red blood corpuscles, which are the corpuscles most commonly used in the Wassermann reaction. If a serum with a low reagin content also contains a large quantity of native amboceptor for sheep cells, the quantitative test with the whole serum or with the 1: 4 dilution may give a Wassermann negative reaction, in spite of the fact that complement has been fixed. A slight trace of complement which remains unbound will suffice to cause hemolysis in the presence of the large amboceptor excess. The same serum, when tested in higher dilutions, such as 1:8 or 1:16 may be Wassermann-positive, since these dilutions may no longer contain enough amboceptor to cause hemolysis, yet may contain sufficient reagin to fix complement. Such a zone reaction is obtained only if the amboceptor and reagin are present in just the proper concentrations. Spinal fluids rarely contain excess amboceptor and rarely give this type of zone reaction.

4. The inhibiting action of serum on complement. This has already been discussed.

FLOCCULATION TESTS

As has already been pointed out, the various flocculation tests which are in existence at the present time differ from each other exactly as the various modifications of the complement fixation tests for syphilis differ from each other. In other words there is no fundamental difference between the different flocculation tests. The differences lie in the variability of adjustment of those factors which determine the sensitivity and specificity of the reaction. However, each modification of the flocculation reaction has been definitely labelled with the name of the originator of the modification, whereas this has not been true in general of the complement fixation reaction. The advantage of so labelling each modification of the flocculation reaction is that the technic of the test is definitely known because it is so named, whereas little is known of a modification of the original Wassermann reaction when it is referred to as "the Wassermann reaction" (which it usually is not if by that term the original Wassermann reaction is under-

stood), or "a modified Wassermann reaction." The only disadvantage, and it does not outweigh the advantage, is that the impression given by so many different names is that each designates a fundamentally different test for syphilis, which is, of course, not true.

Flocculation tests are so called because in general they include both precipitation and agglutination phenomena. They had their beginning in 1907, soon after the development of the Wassermann reaction, when Michaelis observed that a precipitate sometimes formed when the aqueous liver extract used in the Wassermann test was added to syphilitic serum. Jacobsthal in 1910 and Bruck and Hidaka in 1911, found that when an alcoholic extract of either syphilitic liver or guinea pig heart was diluted with salt solution and added to syphilitic serum, microscopically visible aggregates of lipoid particles were formed. Early attempts to modify the conditions of the test in order to make it an adequately sensitive and specific test for the presence of reagin were unsuccessful. These tests assumed diagnostic importance only after the publication of Meinicke's combined water and salt-solution methods in 1917 which was soon followed by the publication of Sachs and Georgi's simplified modification.

The earlier flocculation tests made use of highly diluted serum-antigen mixtures which required long incubation periods to make the aggregates visible and which frequently became contaminated with bacterial growth which made it difficult to differentiate between positive and negative results. Kahn realized these inadequacies of the Meinicke and Sachs-Georgi tests when he was working with them in 1921 (*48*) and began studies directed toward increasing the efficiency of the test. He developed a rapid test which was published in 1922 and which was so superior to the slow precipitation technics that it gained world-wide recognition. The criteria of the Kahn test were high concentration of antigen, the use of undiluted serum, the proper physical state of antigen-salt solution mixture and the proper quantitative relation between serum and antigen-salt solution mixture.

In contrast to the Kahn test, which is an opacification reaction, the Kline, Hinton, and Eagle tests are clarification reactions. The diagnostic criterion of these tests is the clarification of an opalescent suspension instead of the opacification of a translucent "solution."

Great emphasis has been put by most originators of flocculation tests on the simplicity and ease of performance of flocculation tests as compared with the complement fixation tests for syphilis. However, as Eagle (*24*) has pointed out, they have these disadvantages: (1) The large personal factor involved in the reading of weakly positive reactions in which the aggregates are difficult to detect, and (2) the multiplicity of variables which must be rigidly controlled in order to obtain consistent or even reliable results. These two difficulties are masked by the apparent technical simplicity of

the test and only come to light when, on analyzing the results in comparison with the complement fixation test, a high incidence of false positive or false negative reactions is uncovered.

Detailed descriptions of the latest modifications of these flocculation tests have been published in "Technics of Serodiagnostic Tests for Syphilis," Supplement No. 11 to Venereal Disease Information (*124*).

Boerner, Jones and Lukens (*8*) have recently described a simplified microscopic slide test for the diagnosis of syphilis. The antigen is prepared by the simplified method described by the authors for use in the Boerner-Lukens Wassermann technic with slight modification. Aside from the preparation of the antigen, the rest of the procedure is very similar to that of other slide precipitation tests. The authors have also described a macroscopic flocculation test in which the same antigen preparation and emulsion is used.

Kahn (*52*) has recently published a "verification test" which he believes should help to detect false positive reactions obtained in the serodiagnosis of syphilis. The technic is applicable in questionable cases in which serums give doubtful or positive reactions with a diagnostic test. Determinations were made of the effect of different temperatures on the potency of blood serums from animals and human beings. The animal serums were from horses, pigs, chickens, and rabbits and the human serums were from presumably normal persons and from patients with syphilis, leprosy, and other diseases. The technic employed was a precipitation method, similar to that of the standard Kahn test, but was carried out at three different temperatures—37° C., 21° C., and 1° C.

It was found that if serums from syphilitic persons and from apparently normal animals are examined with the standard Kahn test, the precipitation reactions appear identical. If, however, the same serums are tested at 37° C. and at 1° C., differences occur. At 37° C., syphilitic serums show a tendency toward positive reactions and animal serums, toward negative reactions. At 1° C. syphilitic serums show a tendency toward negative reactions and animal serums, toward positive reactions. In serums giving strongly positive reactions, the degree of precipitation was apparently not affected by temperatures of 37° or 1° C. unless the serums are first diluted with physiologic salt solution. Serums of nonsyphilitic rabbits may give strongly positive Kahn reactions. Such serums generally show marked precipitation at both of the differential temperatures. When they are diluted with physiologic salt solution, they show stronger precipitation at 1° C. than at 37° C. whereas syphilitic rabbit serums show stronger precipitation at 37° C. than at 1° C.

Ten human serums giving false positive reactions were studied. The Kahn reactions varied from 3 plus to doubtful in these serums. At 37° C. only 1 of the serums showed precipitation results averaging 2 plus while at

1° C. all the serums showed relatively marked precipitation. The results thus indicated that positive serologic reactions which are unrelated to syphilis, whether given by lower animals or by human beings, can be detected by means of a special precipitation procedure carried out at 37° C. and 1° C. Kahn refers to these reactions as "general biologic reactions."

Among 24 patients with leprosy, 50 percent showed potentialities for the general biologic type of reaction. This type of reaction was noted in isolated cases of syphilis.

Kahn hopes by means of the precipitation technic carried out at 37° C. and 1° C. to decrease the number of false positive reactions and thus assure greater specificity of the test. Serums that give positive reactions with a diagnostic test are examined with this procedure. If precipitation occurs at 37° C. with practically negative results at 1° C. the result is reported "positive" and when precipitation occurs at 1° C. with practically negative results at 37° C. the result is reported "negative." This verification test is intended to be used as a supplementary procedure to diagnostic serologic tests when they give doubtful, weakly, temporarily, or fluctuating positive reactions in cases of asymptomatic syphilis.

QUANTITATIVE COMPLEMENT FIXATION REACTION

The positivity of syphilitic serums shows extreme variations. Some serums contain barely enough reagin to give a positive or doubtful reaction when 0.2 cc. of undiluted serum is used in the test, while others contain 100 to 400 times this minimal quantity (reagin units). For ordinary diagnostic work the exact quantity of reagin is of no importance as long as it is sufficient to give a positive reaction in the presence of syphilis. A patient whose serum is positive up to a 1:10 dilution (reagin titer of 10) is no less syphilitic than a patient whose serum is positive up to a 1:800 dilution. According to Eagle (*27*) it is not yet known whether the reagin titer has any prognostic significance, the evidence available at the present time indicating that it has no significance of this sort. The routine qualitative test is therefore completely satisfactory for diagnosis.

Moore and Eagle (*95*) applied the quantitative Eagle complement fixation test to the serologic study of 508 cases of early and 1,159 cases of late syphilis. Their arbitrary definition of reagin titer is the highest dilution of serum which gives a positive result, for example, if the reaction is positive with serum diluted 1:2 but negative in 1:4 and higher dilutions, there are said to be 2 units of reagin. All of the cases of early syphilis studied had received no treatment, whereas of the late cases only 445 had received no treatment.

The reagin content of the blood was found to be much higher in early than in late syphilis. In the early weeks of infection there was found to be a progressive increase in titer until the appearance of secondary manifesta-

tions. Thereafter the median titer remained approximately unchanged during the secondary stage. In later years of syphilitic infection and whether or not treatment had been given, the titer was found to fall gradually or abruptly and in all types of late syphilis was from $\frac{1}{5}$ to $\frac{1}{10}$ as great as in the early months. In all stages of syphilis, even during the secondary stage, there were wide individual variations in reagin content. Previous treatment, regardless of amount or of the time interval between its administration and the performance of these serologic tests, may markedly reduce the serum reagin content, even though clinical improvement does not occur.

The authors conclude from this study that quantitative serologic testing is of little or no value in the routine serologic diagnosis of syphilis.

There are, however, special phases in the diagnosis and treatment of syphilis in which it is of great importance to make quantitative measurements of positivity. Such a quantitative test is made on serial dilutions of serum, and the maximal dilution which gives a definitely positive result is reported.

Quantitative reactions with the complement fixation test as well as with the flocculation tests are of importance in determining the effect of treatment on the reagin titer. If only a qualitative test is done on a patient who at the beginning of treatment had a very high reagin titer, it might happen that after he had received considerable antisyphilitic treatment the qualitative test would still show his blood to be strongly positive. If, however, quantitative determinations of reagin content were done, it would be seen that in many cases which apparently show no serologic response to treatment, the reagin titer has, as a matter of fact, been markedly decreased in spite of the fact that sufficient reagin still remains to give a strongly positive qualitative test. The quantitative test, therefore, measures the amount of the decrease that has occurred in reagin content as a result of treatment. It may also prove to be of value in determining the efficacy of various methods of treatment. Finally, it may indicate the appearance of a relapse. Kahn (*51*) states that instances have been observed in which a sudden rise in the titer during treatment proved to be the forerunner of a relapse. This rise in the titer may precede the relapse by several weeks.

Moore, Hardy, Robinson and Eagle (*94*) studied the response of the quantitatively titered "Wassermann" test in early syphilis to treatment with arsphenamine (78 patients), neoarsphenamine (74 patients), silver arsphenamine (35 patients), mapharsen (81 patients), and bismarsen (21 patients). Their definition of a reagin unit was the same in this study as that already described in connection with a discussion of Moore and Eagle's most recent study. They pointed out that the reagin titer of patients with early syphilis before treatment varies between 12 and 3,200 units but that in the majority of cases it is between 100 and 400 units.

The method they used was to perform a quantitative complement fixation test on each patient's blood before treatment and at the time of administration of each dose of the several drugs studied. In the majority of patients studied, 8 weekly (bismarsen twice weekly) injections of drug were given, and 8 titered complement fixation tests were performed; all of the patients included had at least 4 titered tests. All of the patients had either primary seropositive or early secondary syphilis. It was found that in some patients, the trend of the quantitative test during treatment was progressively toward negative whereas in others wide variations in the reagin titer were observed. As far as the rate of Wassermann reversal was concerned, the 5 drugs studied were approximately equal. The authors concluded from this study that the rate of Wassermann reversal is not an adequate method of determining the relative ultimate worth of drugs of the arsphenamine serics.

The quantitative spinal fluid Wassermann reaction has been found to be of definite prognostic and therapeutic significance and has, therefore, been adopted almost universally. In general, the reagin content of the fluid reflects the degree of central nervous system involvement. The rate at which this reagin titer falls under treatment is often the only real index of the effectiveness of treatment.

Another very important application of the quantitative test is in determining whether an infant has been infected by its syphilitic mother or whether it has escaped such infection. This cannot be determined by making one or several diagnostic (qualitative) serologic tests soon after birth, because it is not uncommon that a passive transmission of reagin from the serologically positive mother to the infant occurs, giving an uninfected infant a positive blood reaction (Fildes' law). This reaginemia in the infant, particularly when it occurs following adequate treatment of the mother during the pregnancy (which treatment may or may not have rendered the mother seronegative) disappears and the infant's blood becomes negative without treatment. In such cases the quantitative test is of great value because by means of it the gradual dccrease of the reagin titer can be followed. If, however, the infant is definitely infected with syphilis, many factors such as immunologic immaturity of the infant, late intrauterine infection, or treatment of the mother may delay the production of sufficient reagin in the blood of the ncwborn infant so that at first it will not be demonstrable by even the more sensitive test. By means of the quantitative Wassermann test, which is repeated over a certain period of time, a gradually increasing reagin titer is indicative of the actual presence of syphilitic infection.

Dunham (*22*) reported the following procedure used in the diagnosis of congenital syphilis of the newborn. A Wassermann test of the blood is made a day or two after birth. If the reaction is positive the test is repeated in a few days and again before discharge from the hospital at 10 days or 2 weeks

after birth. If on the second test the Wassermann reaction remains positive but is weaker, treatment is still withheld. At the third test the reaction will usually have become still weaker or even negative if the infant has not been infected with syphilis, and treatment may still be withheld. In those cases in which the second test does not show a weaker reaction than the first and does not become still weaker at the end of 10 days, the infant is regarded as syphilitic and treatment is begun. In cases in which the mother is willing to cooperate in bringing the infant back for examination it is suggested that the period of observation be prolonged beyond 10 days. Dunham reported observations on 14 infants with originally positive Wassermann reactions. They were observed for from 2 months to 4 years, and none of them developed any evidence of syphilis.

Roby and Lembcke (*106*) in discussing the meaning and reliability of umbilical cord Wassermann tests pointed out that the umbilical cord Wassermann reaction reflects almost exactly the condition of the mother's blood at the time of labor. If the mother's blood is negative, the cord blood will be negative, if positive, the cord blood will be equally positive. The substance causing the positive Wassermann reaction passes out of the child's blood in most cases by the end of 2 months, leaving the child's blood a frank negative, provided the child actually does not have syphilis. If the child actually has syphilis the Wassermann reaction remains as strongly positive after a number of days and weeks as it was in the cord blood. The decreasing Wassermann reaction means that the child does not have syphilis and that treatment should be withheld.

Faber and Black (*30*) applied the quantitative complement fixation test to the study of 10 infants. Two of these infants were syphilitic, and 8 were presumably nonsyphilitic. In 7 of these 8 the reaction to the initial routine Wassermann test was 3 plus, it being 2 plus in one of the infants. Only 1 or 2 units of reagin were found in these 8 infants except in 1 case in which 40 units were found on first examination. A unit of reagin is defined by these authors as the amount of reagin that in 0.1 cc. of serum is just sufficient to give a positive Wassermann reaction. It was found that the reagin had disappeared from the blood of the presumably nonsyphilitic infants by the end of the first week or sooner with the exception of the infant who had had the high initial reagin titer. In this infant a sharp reduction in the titer occurred on the 7th day. In this case the progressive but very gradual decline was striking. When determined by the ordinary method, the Wassermann reaction remained 3 plus as late as the 52d day and was still 2 plus on the 73d day. The reagin titer which declined more suddenly at first nevertheless did not reach zero until the 94th day. Of the two syphilitic infants, 1 died a few hours after birth and the other, two days after birth. The cord blood of one of these and the blood of the other obtained on the day of birth showed a reagin content of more than 160

units. The authors concluded from this study that the quantitative method used in the complement fixation test in which the amount of reagin present is measured is a valuable means of distinguishing between those infants who have merely a reaginemia and those who actually have a syphilitic infection. In the former the amount of reagin which is usually, but not always, small, progressively declines to zero.

Christie (*14*) reported the study of 14 infants whose quantitative blood Wassermann reactions, using the method of Faber and Black, were found to be positive on the 7th or 8th day of life. These quantitative tests were repeated periodically for 4 months or longer with the result that in 11 infants two or more negative reactions were finally obtained whereas in 3 infants the reactions remained positive. In all of these cases repeated quantitative Wassermann tests, physical examinations, and roentgenograms of the bones were taken at frequent intervals during the period of observation. The Wassermann reaction of the blood of all the mothers of the group of 11 cases was positive, and in all of the cases the mother had received some antisyphilitic treatment. The cord blood was positive in all except one case, in which the specimen hemolyzed. The quantitative reaction of the infants' blood, which had initially been positive, became weaker, reversing to negative in periods varying from 22 days in 2 cases to 86 days in 2 other cases. These periods of from 22 to 86 days, with an average time for the 11 cases of 55 days, represent the time during which the reagin, which had entered the blood of the infants by passive transfer through the placenta, disappeared from the blood of these infants.

In 1 of the 3 cases in which the initial quantitative Wassermann titer rose, the blood increased gradually until the 59th day, when clinical evidences of syphilis were present. In another case only two tests were made, on the 5th and on the 66th day. The titer had increased on the second examination. At this time clinical and roentgenologic signs of syphilis were also present. In the third case the titer fell gradually until the 46th day. On this day, however, clinical signs suggestive but not pathognomonic of syphilis appeared, and the quantitative test was strongly positive. This case illustrates the limitations of this method for making a definite and early diagnosis of syphilis before clinical or roentgen-ray signs appear.

Davies (*20*) studied the serologic reactions of 56 infants born of syphilitic mothers. Forty of these infants were 12 months old, 12 were 6 to 12 months old, and 4 were 4 to 6 months old before the study was closed. They were given careful physical examinations at birth and at the time of discharge from the maternity hospital. An attempt was made to secure a regular Hinton test for syphilis and roentgen-ray films of the long bones within the first week after birth. The strength of the serologic reactions was determined by the capillary Davies-Hinton test. Ten nonsyphilitic infants were used as controls. The infants were examined at the age of 6 weeks, 3 months,

and 1 year. In spite of special efforts, only 22 were considered to have satisfactory follow-up records. Only two of the infants were found to have syphilis. The mothers of both of these infants had strongly positive serologic reactions. It was found that in most instances the transmitted positive reaction in the blood of the infants diminished or disappeared within 2 weeks after birth, but in 1 case it was present for 40 days and in another case, for 3 months. Both of these infants were kept under observation for more than 1 year and at that time were discharged as nonsyphilitic.

As Kahn (*51*) and also Moore (*93*) have pointed out the quantitative reaction is of value in the diagnosis of questionable cases when patients give no history or clinical evidence of syphilis. In case of doubt in regard to the diagnosis of syphilis because of doubtful or weakly positive serologic reactions with conflicting results from different laboratories and with different technics, Moore advises prolonged serologic follow-up, without antisyphilitic treatment, by means of a good quantitative technic. The patient is probably not syphilitic if his serum shows a markedly fluctuating or spontaneously falling titer. Kahn points out that insufficient records are available in regard to the diagnostic value of positive serologic reactions accompanied by high titers as compared with positive reactions accompanied by low titers but that it would seem reasonable to assume that high titers are of greater diagnostic value (in the absence of a history and clinical evidence) than low titers. Kahn also states that the quantitative reaction should prove of value in the diagnosis if there is a history or clinical evidence of syphilis. He says that all indications are that low, moderate, and high titers correspond in most instances to low, moderate, and marked syphilitic activity. An outstanding exception to this generalization is when the patient is literally overwhelmed by the spirochetes and an excessive amount of antigenic material is thrown into the circulation. When this occurs, antigen-antibody union may take place in vivo, causing the antibody titer to drop. Kahn further advises that the quantitative reaction be employed in all conditions in which positive serologic reactions are obtained in the absence of syphilis, pointing out that it would prove of great importance to establish the titers of positive reacting serums in leprosy, malaria, infectious mononucleosis, and other nonsyphilitic diseases. The indications are that the titer in these diseases is low, but no experimental evidence is available.

EXAMINATION OF CEREBROSPINAL FLUID

Although in the examination of cerebrospinal fluid the complement fixation or flocculation reactions are the only specific tests for the reagin produced by the syphilitic infection, there are a number of auxiliary tests which are routinely applied. Since they are not specific, their chief value lies in the fact that they indicate the extent of the pathologic involvement

of the central nervous system. They are therefore important in the prognosis of the disease because they are sensitive indicators of the extent of the pathologic change which exists.

A detailed discussion of these tests does not lie within the scope of this paper. They are to be considered only in regard to their relationship to the tests for reagin in the spinal fluid. The most important of these auxiliary tests are the cell count, qualitative and quantitative tests for total protein and globulin, the quantity of albumin being determined by subtracting the globulin from the total protein, and the colloidal reactions. The spinal fluid findings in various clinical types of neurosyphilis in comparison to the normal findings are succinctly outlined in a table by Moore (*90*).

There is some disagreement in regard to the number of cells present in normal fluid, some writers believing that no cells should normally be seen while others regard 10 per cmm. as the upper limit of normal. From 5 to 10 cells constitutes a slight, from 10 to 50 a moderate, from 50 to 250 a severe, and more than 250 cells an extreme pleocytosis (*56*). Different figures for the normal values have been given for total protein content, some considering 25 mg. percent and others, 75 mg. percent as the upper limits of normal.

Lange, who introduced the colloidal gold test for syphilis, and many others after him, regarded the various types of reaction as entirely due to variations in the protein content of which the test was thought to be an indirect means of quantitative measurement. Further studies have shown however, that the explanation of this reaction is not quite so simple. There are several proteins present in spinal fluid, such as albumin, euglobulin, and pseudoglobulin, and there is evidence suggesting that variations in different combinations of these proteins and perhaps in the number and types of cells are important factors in the production of colloidal reactions. It is probable that the globulin is a predominant factor. It has been shown, for example, that the globulin which is first precipitated from syphilitic spinal fluid and then redissolved in saline, can produce the same reaction as the whole spinal fluid, that the substance producing the reaction is not the same as the substance producing the positive Wassermann reaction and that the albumin tends to protect the colloidal gold solution from the precipitating action of the globulin. Kafka and Samson (*46*) found that pure solutions of albumin have no effect on the colloidal mastic reaction, but when added to globulin solutions, the albumin has a protective function. However, Kafka (*47*) has found by means of quantitative determinations of total protein, globulin, and albumin, that in the presence of a considerable increase of globulin a negative colloidal gold curve may be obtained. This phenomenon was more frequently observed in nonsyphilitic disease of the brain and in syphilis without brain involvement than in neurosyphilis.

Kafka points out that other so-called dissociations have been previously described in the literature, for example, an increase in protein content with no increase in the cell count, an increased cell count with slight or no increase in the amount of globulin or in total protein, and a positive colloidal gold reaction with no increase in total protein. In general paresis it is chiefly or only the globulin fraction which is increased, there being in only about half of the cases a slight increase of albumin and in some cases even a decrease in the albumin content. In taboparesis, tabes, and cerebrospinal syphilis, the albumin is increased together with the globulin.

Although the colloidal reactions (colloidal gold and colloidal mastic tests are considered to be of equal value) give different curves for different types of central nervous system syphilis, in single cases the curve is by no means always typical for the group to which the case belongs. Marchionini, (*79*), who examined 2,000 spinal fluids, found that only 57 percent of the cases of general paresis, only 36 percent of the cases of tabes, and only 66 percent of the cases of cerebrospinal syphilis had curves which were characteristic of the group to which they belonged. Menninger and Bromberg (*83, 84*), who examined the spinal fluids of 500 cases of neurosyphilis, found that in 71.1 percent of cases of general paresis, 57.8 percent of cases of taboparesis, and 39 percent of cases of tabes, as well as 28.9 percent of cases of asymptomatic neurosyphilis, the curve was of the so-called paretic type. Novy (*98*), who also examined the spinal fluid of 500 cases of neurosyphilis, found a "paretic" curve in 65 percent of cases of general paresis, 32 percent of cases of taboparesis, and 11 percent of tabes.

In view of these findings it is repeatedly pointed out that a differential diagnosis of syphilis of the central nervous system cannot be made solely on the basis of the colloidal tests. Kilduffe (*56*) states that a diagnosis of general paresis should never be made unless, in addition to the "paretic" colloidal gold curve, increased globulin content, increased cell count and positive blood and spinal fluid Wassermann reactions are also found. Stokes (*120*) points out that a spinal fluid which is absolutely normal to protein, colloidal test and cell count, with a strongly positive Wassermann reaction in one or all concentrations, is almost undoubtedly a technically false positive and the examination should be repeated and checked against clinical findings. In regard to their value as spinal fluid tests for syphilis, Stokes rates the different tests in the following order according to their relative importance: (1) Wassermann reaction, (2) cell count, (3) colloidal gold reaction, and (4) globulin content.

Some interesting observations on the relationship of the Wassermann reaction, cell and globulin content, and colloidal gold reaction of the spinal fluid in patients with syphilis, chiefly neurosyphilis, were made by Thjötta and Saethre (*125*). They compared the reactions on 200 spinal fluids obtained partly from patients with neurosyphilis and partly from patients

with latent syphilis. Striking differences were found between treated an untreated cases. In the untreated cases a negative or weakly positiv Wassermann reaction was found to be accompanied by a low cell count, lo albumin content, and slightly positive colloidal gold reactions. In th untreated cases a strongly positive Wassermann reaction coincided wit a very high cell count and marked increase in globulin and colloid gold reactions, while a positive and weakly positive Wassermann reactio occurred together with lower figures for the other reactions. This agreemer between the reactions occurred in 83.2 percent whereas some degree of dis greement was found in 16.8 percent. A positive Wassermann reactio without other pathologic findings in the fluid was never observed to occu The causes of disagreement among the various reactions were: (1) relatively too high cell count. This was the most frequent cause of dis greement, occurring in 8 out of 125 cases. In 7 of these the clinical diagnos was cerebrospinal syphilis. (2) A relatively high albumin and globuli content which occurred in 5 fluids with "manifest neurosyphilis." Th colloidal gold reaction never occurred as an isolated pathologic findin It was negative in 81.5 percent of fluids which showed a negative Wasse mann reaction. Paretic curves were found in more than three-fourths of th spinal fluids which gave strongly positive Wassermann reactions. Ther were 2 cases of cerebrospinal syphilis and 1 of hemiplegia which showe positive colloidal gold reactions and negative Wassermann reactions.

Treated cases were defined as those which had received arsphenamine c bismuth treatment during the course of the 6 months preceding this stud It was found that the cell count and globulin values were much lower tha in the untreated group. Fluids with negative Wassermann reactio showed many pathologic colloidal gold curves. Among the fluids wit moderately positive Wassermann reactions, positive colloidal gold curv were almost as numerous as among the untreated cases. In other word treatment definitely influences the cell count and globulin-albumi reactions but has little effect on the Wassermann and colloidal gol reactions, especially the latter. Essentially the same observations o spinal fluid findings have been made by many other workers followin treatment with malaria (*126*) and with tryparsamide (*44*).

Effect of contamination of the spinal fluid with blood on spinal fluid reactions.— Solomon, Dailey and Fremont-Smith (*115*) have described methods b means of which a corrected cell count, protein, sugar and chloride deter mination, and colloidal gold reaction can be obtained in spinal fluid whic is accidentally contaminated with blood. They point out, however, tha in the presence of a positive blood serologic reaction, a positive reaction i contaminated cerebrospinal fluid is of no value. Only a negative reactio is significant.

Foord and Bauckus (*32*) found that as little as 0.01 cc. of positive serun

n 2 cc. of normal cerebrospinal fluid imparts enough reagin to give a lightly positive Wassermann reaction and that as little as 0.04 cc. will mpart a 4-plus reaction to negative spinal fluid. They advise that in xamining spinal fluid from patients with a positive blood Wassermann eaction, fluids containing traumatic blood in grossly visible amounts hould not be used.

Loveman and Stocking (*77*) studied the Kahn reaction in spinal fluids ontaining varying amounts of syphilitic blood. They added 100 blood erums of patients with syphilis to spinal fluids known to give a negative eaction. The exact amount of serum necessary to convert these spinal luids to positively reacting fluids was then determined. The results aried from as much as 8 drops to as little as $\frac{1}{28}$ drop, this variation depending on the potency of the syphilitic blood as measured by the quantitative Kahn reaction. In order to ascertain whether any product of hemolysis ffected the serum of the spinal fluid, the blood of 22 syphilitic and 26 nonyphilitic patients was collected. The serum was removed with saline olution, the cells were lysed in distilled water, and the cellular debris was emoved by centrifugation; after this the hemolysed fluid was added to pinal fluids known to give a negative reaction. The fluids were tested in he usual manner and gave uniformly negative results. The authors conluded from this that if the Kahn test of the spinal fluid containing blood s positive, another lumbar puncture is indicated. According to their indings the substance responsible for the serologic change in spinal fluid ontaminated with blood is present in the blood serum and not in the rythrocytes.

SEROLOGIC REACTIONS IN THE DIAGNOSIS, TREATMENT, AND PROGNOSIS OF SYPHILIS

In primary syphilis the diagnostic method of choice is the dark-field examination, since serologic tests on the blood do not become positive until the end of the second week and in exceptional cases not until 3 months after the appearance of the chancre. In case the dark-field examination is repeatedly negative and the blood tests are also negative, serologic follow-up is indicated, regardless of the characteristics of the lesion. During this period of observation, blood tests should be taken once or twice weekly. Stokes (*120*) advocates that the final follow-up serologic test should be taken 4 months after the appearance of the lesion.

According to Stokes the serologic reactions are positive in 35 to 50 percent of cases of primary syphilis by the end of the second week. From this time on there is a steady increase until at the end of the 8th week 80 percent or more of cases have positive serum reactions.

Kline, Littman and van Cleve (*60*) applied the Kline test to the examination of 94 venereal and 12 nonvenereal sores with control clinical observa-

tions, blood tests, dark-field examinations, and examinations of staine smears. They observed that nonspecific sore fluids which were turbi with exudate frequently gave positive results. This was also true of non syphilitic sore fluids containing any appreciable quantity of antisepti soaps, solutions, and salves. It was found, however, that when blooc even in a considerable quantity was present, the results in syphilitic an nonsyphilitic cases were satisfactory. In fact, it seemed quite possibl that the positive results of sore-fluid tests depended on the presence c blood squeezed from injured vessels rather than on reagin in an extra vascular fluid of the sore itself. This impression was strengthened by th fact that blood-tinged and bloody sore fluids obtained from cases havin tertiary syphilis gave positive results (blood drawn from the arm vein a the same time likewise giving positive results) in contrast to negative reacting sore fluids obtained from individuals free from syphilis. The concluded that more experience would be required to evaluate properl the sore-fluid tests but state that the sore fluid does not compare favorabl with blood for testing for syphilis because even small quantities of advent tious substances may cause it to give false positive results.

The dark-field examination is also of importance in the diagnosis of sec ondary syphilis with a negative blood Wassermann reaction (an infrequer finding) especially if no history of exposure can be obtained and there no chancre. The Cooperative Clinical Group (*119*) found that in 90.7 pe cent of condylomatous genital lesions, 85.6 percent of mouth and throa lesions, and 79.3 percent of all cutaneous lesions including condyloma dark-field examinations were positive. The serologic tests are so often pos tive in secondary syphilis that the diagnosis can be said to be a laborator problem. From 92 to 99 percent of patients with secondary syphilis hav positive serologic reactions.

Moore and Kemp (*88*) made a statistical study of the Wassermann reac tions in a group of 879 patients treated for early syphilis. This study in cluded material extending over a period of 10 years. The Wasserman test used did not make use of ice-box incubation. These patients had re ceived at least 4 injections of arsphenamine and had had 4 consecutiv Wassermann records at regular intervals. In a group of 110 seronegativ primary cases, there were 18 (16.3 percent) in which some degree of Wa sermann fixation developed within a week after the first arsphenamine injec tion, and in 9 of these the reaction became completely positive. Follow ing this, the reactions became gradually less positive and were negativ by the seventh week of treatment.

In the seropositive primary and early secondary groups, the provocativ phenomenon was absent because in most of the patients the test was com pletely positive at the outset. But in 31 (53.3 percent of 57 cases of earl

econdary syphilis) there was an increase in titer following the first arsphenmine injection.

It was found that individual cases of early syphilis showed considerable ariation in the rapidity with which the Wassermann reaction became nd remained negative. In 31.4 percent of seropositive primary and in 9.5 percent of early secondary syphilis, two injections were found to uffice to change the Wassermann reaction from positive to negative. The uthors state that in both groups, a negative Wassermann reaction may be xpected as the result of a single course of arsphenamine in approximately 5 percent of all cases. The weekly injections of arsphenamine were given n doses of 0.4 gm. for men and 0.3 gm. for women.

Fifty patients with early secondary syphilis were given continuous treatnent consisting of 4 or more courses of arsphenamine with interim mercury nd potassium iodide. The record of each patient included at least 24 eparate Wassermann tests performed over a period of about 1 year. For ll practical purposes, all trace of complement fixation had disappeared y the third course of arsphenamine (the 28th week of treatment). The ubsequent clinical outcome after one or more years of observation without reatment was determined in 21 of these 50 patients. In none of these did linical recurrence of the secondary type nor Wassermann recurrence take lace. Twenty were regarded as probably cured whereas in one central ervous system syphilis developed.

Another series of patients failed to cooperate in receiving continuous reatment and therefore had periods of treatment alternating with periods f rest. The Wassermann curve in this group is in striking contrast to that f patients receiving continuous treatment. During every interval without reatment, the Wassermann reaction tends to revert to positive. The esponse of the test to the second arsphenamine course is not so prompt as rom the first course and tends to become even less in subsequent courses. The rise toward positive is almost as great during each lapse from treatnent. When a lapse in treatment, lasting an average of 7½ months, occurred etween the first and second arsphenamine courses, recurrent positive Wassermann reactions were 10 times as frequent as when treatment was ontinued without interruption. Clinical recurrences of a secondary type eveloped in 30, or 11.8 percent of patients treated intermittently, as ontrasted with only 6, or 2.6 percent of those who received 2 courses of arsphenamine with mercury given between courses. A lapse between the econd and third treatment courses was also attended by a tenfold incidence f Wassermann recurrences. The authors estimate that cure is 3 times as requent in patients who receive continuous treatment as in those treated intermittently, whereas the reverse is true of recurrent secondary or latent syphilis.

Among variations from the average Wassermann curve, persistent Wasse mann positivity, prematurely negative Wassermanns, and seronegati secondary syphilis are discussed.

In 117 patients with seropositive primary or early secondary syphilis whom the Wassermann reaction was completely positive before treatmer the reaction became and remained negative following one or two doses arsphenamine. This occurred in 36 patients following a single injectio and in 82 after 2 injections. It was found that recurrences of a seconda type occurred 4 times as frequently in the prematurely negative Wasse mann group (30.5 percent) as in the average patient whose Wassermai response to treatment is less rapid (8.6 percent).

Among 618 patients with early secondary syphilis, the Wassermai reaction was positive before treatment in 561 (90.77 percent). A su gestive positive result (75 percent fixation) was obtained in 24 patier (3.89 percent), doubtful in 14 (2.26 percent), suggestive negative in (1.77 percent), and frankly negative in 8 (1.29 percent), making a total 57 patients in whom the Wassermann reaction showed incomplete fixati before any treatment. The authors state that the explanation of this failu of the reaction to become completely positive cannot be related to the ty or extent of early lesions present nor to the influence of sex, but that th type of Wassermann response depends on the same factors responsible f the "prematurely negative" Wassermann group, namely, an inherent la of resistance against infection. Under similar conditions of treatment was found that recurrences of a secondary type were 5 times as frequent this group of 57 patients (45 percent) as in the standard group (8.7 percen The authors point out that in such cases it is even more essential than usu that treatment be intensive and continuous so that treponemicidal drus may accomplish the destruction of organisms which the patient is unab to deal with himself.

Persistent Wassermann positivity will be discussed later.

The Cooperative Clinical Group (*119*) found that, among patients wi early syphilis treated with arsphenamine alone, the continuous meth secured the reversal of the blood Wassermann reaction by the end of year in 91.2 percent whereas the intermittent scheme of treatment wi arsphenamine alone and rest intervals of a month or more resulted in or 58.5 percent of reversals, and irregular treatment with arsphenamine alo gave only 9.3 percent of Wassermann reversals to negative within a ye Wassermann reversal occurred within the first 3 months by arsphenami alone in 83.5 percent of all patients with early syphilis. This agrees ve well with Moore and Kemp's finding that, in patients with seropositi primary and early secondary syphilis, the blood Wassermann reacti became negative after 6 to 8 injections of arsphenamine in 85 perce Intermittent and irregular treatment were found to be the principal sour

f delayed reversal of the blood Wassermann in point of time, 24 percent f these cases requiring over 2½ years for the reaction to reverse under regular, 4 percent under intermittent, and only 1.5 percent under con-nuous treatment. There was also a definite relationship between resistant ositive serologic reactions and the tendency to clinical relapse. The total f relapses in patients always negative or reversed to negative within the rst year was only 22.5 percent as compared with 48.1 percent in patients /hose serologic reactions showed delayed reversal. Among 129 patients /ith early latency the Wassermann reaction was reversed to negative after ıe first course of treatment in 44 (34.1 percent) and in 291 patients with ıte latency in 70 (24 percent).

A study of patients with early and late latency (*89*) who received two or ıore courses of arsphenamine either by the continuous or the intermittent ıethod showed that in both early and late latency Wassermann reversal ; obtained approximately as frequently with intermittent as with continuous reatment. Wassermann-fastness in both groups was more frequent under ontinuous treatment and Wassermann-relapse more frequent under inter-ıittent treatment. However, considering the two phenomena of fastness nd relapse together, their frequency was found to be approximately the ame whether treatment was continuous (63.9 percent) or intermittent (62.9 ercent).

On the basis of clinical outcome, continuous treatment in early latency vas found to be as desirable as in early syphilis, but in late latency it did ıot seem to be imperative. It was found that a satisfactory clinical out-ome was obtained in 43 percent of patients treated continuously as against 7 percent of those treated intermittently and that clinical relapse and Wassermann-fastness were approximately twice as common in the inter-nittent as in the continuous group. The time necessary for the develop-nent of true latency and of maximum resistance is variable but is prob-bly always complete within 4 years. After this has occurred, the Wasser-nann curves for late latency indicate that treatment, whether continuous or ntermittent, will not disturb the immunologic relationships already estab-ished and that the character of treatments, provided it is sufficiently pro-onged, makes little real difference in either clinical or serologic outcome.

A generalized mucocutaneous relapse is accompanied by Wassermann ositivity in 87 percent, a localized relapse by Wassermann positivity in 55 ercent if the eye is involved and in 34 percent if the nervous system is nvolved.

In latent syphilis, on the contrary, clinical and serologic relapse usually lo not coincide. The former is rare, the latter common.

Stokes (*120*) has found the blood Wassermann reaction to be negative in ıs high as 59 percent of neurosyphilitics in general. Nonne (quoted by Stokes) estimated that in 30 to 40 percent of cases of tabes the blood serologic

reactions are negative, and Gennerich estimated that this was true in 50 t
60 percent of cases. The consensus of opinion is that the blood Wasser
mann test is positive in from 90 to 100 percent of cases of general paresi
Cases of general paresis in which the blood reactions were negative have
however, been observed to occur. In vascular neurosyphilis the blood Was
sermann is usually positive but may be negative.

False Positive Reactions

False positive reactions are of two kinds, namely, technical false positive
which are due to some error in the performance of the test, and biologi
false positives which occur in conditions other than syphilis. Only th
biologic false positive reactions will be discussed. All that needs to be sai
in regard to the technical false positive reactions is that since they do oc
cur, a diagnosis of syphilis in the absence of a history or clinical findings
syphilis should never be made on the basis of one positive test. If a positiv
reaction is obtained in such a case, the test should be repeated in the sam
laboratory or in another laboratory and preferably more than one type
test should be done on this second specimen.

Diseases which definitely give false positive reactions for syphilis are yaw
relapsing fever, and trypanosomiasis. Since these diseases do not occu
in temperate zones, they need not be considered in detail. Other diseas
and conditions in which false positive serologic reactions occur are lepros
malaria, tuberculosis, infectious mononucleosis, and febrile diseases.

Leprosy.—Kolmer and Denney (*63*) in 1923 reported that with the ol
Wassermann technic apparently false positive reactions occurred in 7
percent of patients with leprosy but that the Kolmer modification did n
give false positive reactions in leprosy. This was based on a study of 1
cases of leprosy. Yagle and Kolmer (*131*) in 1923 applied the Kahn te
to 28 cases of leprosy and concluded that in leprosy uncomplicated l
syphilis the Kahn test gave negative reactions. However, the evaluatic
study of serologic tests in the United States (*17*) in 1935 showed that in
group of 50 patients with leprosy the Kolmer test gave 64 percent and th
Kahn test 60 percent of false positive reactions. The Eagle flocculatic
test gave 72 percent, the Kline test 66 percent, and the Hinton test 40 pe
cent of positive reactions for this same group. More careful study of the
50 patients, including a study of the long bones and the aorta for the excl
sion of syphilis, and repetition of the serologic tests was made (*38*). In th
second study 15 patients (30 percent) had positive or doubtful reactions
all tests; 4 (8 percent) had uniformly negative reactions, and 31 (62 percen
showed discrepant results with the different tests.

Malaria.—Extremely variable reports can be found in the literature
regard to the incidence of positive serologic reactions for syphilis which occ
in patients with malaria. According to the 1935 official evaluation stu

(*17*) the Kolmer test gave 19.4 percent, the Kline test 14.3 percent, the Eagle flocculation test 12.1 percent, the Kahn test 11.4 percent, and the Hinton test 11.1 percent of positive reactions in 36 patients with malaria. In 1938 (*41*) a second evaluation study of 266 white patients with malaria was made. The percentage of positive reports, although not as high as in the first study, was higher than would be expected among white persons who are presumably nonsyphilitic. The percentage of positive reports was 4.4 for the Hinton, 4.9 for the Kolmer, 6.2 for the Kline diagnostic, and 16.2 for the Kline exclusion tests. Besides this, there were a number of doubtful reports with all except the Kolmer test.

Eller (*29*) points out that the nature and the regularity of the appearance of a positive Wassermann reaction in certain stages of inoculation malaria leads to the assumption that the processes which bring about the positive reaction are similar to those of syphilis. Nagell and Langhans (*97*) state that the reason for the difference of opinion in regard to the effect of malaria on the Wassermann reaction among various authors is due to the fact that these authors could not definitely exclude the presence of latent syphilis. Nagell and Langhans report on the serologic reactions of 10 cases of gonorrhea which were treated with inoculation malaria and in whom syphilis was definitely ruled out. In 9 out of the 10 patients the complement fixation test for syphilis was completely positive between the fifth and ninth chill, but 7 to 15 days after the last chill (quinine was always given to stop the chills) the Wassermann reactions became again negative. Kuske (*72*) found that nearly 100 percent of nonsyphilitic persons who were inoculated with malaria showed positive serum reactions for syphilis. After a variable period of complete positivity, the reactions again returned to negative. Parallel changes in the spinal fluid did not occur. Taussig and Orgel(*123*), who studied 154 cases of malaria in St. Louis, found 21 percent of false positive reactions among these patients in whom syphilitic infection was ruled out as compared to 5.5 percent for the general population and to 15 percent for the city hospital. Saunders and Turner (*112*) found no positive reactions in 135 malaria patients in whom syphilis and yaws could be ruled out. According to Fischer and Günsberger (*31*), the positive Wassermann reaction in malaria is due to the presence of specific antibodies against erythrocyte lipoids. They found that among 28 serums obtained from malaria patients there were 21 with definite to completely positive complement fixation with erythrocyte extract. With a few exceptions, 500 Wassermann negative serums from healthy persons and patients reacted negatively. Among 60 Wassermann positive syphilitic serums there were some which also reacted with the erythrocyte extract, but these could be differentiated from those of malaria patients by considering the quantitative reaction to erythrocyte extract and Wassermann extracts. They concluded that when the Wassermann and the erythrocyte reaction are carried out simul-

taneously, Wassermann positive malaria can be definitely differentiated from syphilis.

Tuberculosis.—There is also considerable difference of opinion in regard to the effect of tubereulous infeetion on the Wassermann reaction. In the 1935 evaluation study the percentages of positive reaetions obtained in 5 eases of tubereulosis were Hinton 5.7, Kolmer 2.0, Kahn, Kline, and Eagle (floeculation) tests each 1.9. The findings of a special committee to study the effeet of tuberculosis on the serologic reaetions for syphilis was reported by Parran and Emerson (*103*) in 1939. Eight serums out of 458 serums o supposedly nonsyphilitic tuberculous donors which were contributed by sanatoria were found to be positive to many tests. Four of these were found to be probably syphilitie, 3 were not available for reexamination and in 1 no evidenee of syphilis whatsoever could be found. The author state that "it seems justifiable to omit all of the 8 cases from the final tabulation." Whether this is justifiable, in view of the fact that 4 of them (whieh could not be reexamined and 1 in whom no evidence of syphili could be found on reexamination) could certainly not be said to be syphiliti and that in the remaining 4 the diagnosis of syphilis was only probable, questionable. In the remaining 450 serums, 1 positive result was obtaine with the Eagle macrofloeculation test, 4 positives with the Hinton, 1 positive with the Kahn presumptive, and 5 positives with the Kline exclusion The Kolmer and Kahn standard tests gave negative results. Those tes giving positive results also gave a number of doubtful results. It was note that some positive and doubtful results beeame negative on repetition the test. The committee eoneluded that "tubereulous toxemia may eontribute a eonfusing faetor to syphilis serology."

Stokes (*118*) states that in his experienee latent tubereulosis is apparent responsible for false positive serologic reactions. He cites the case of virgin Catholic nun who came to autopsy and was found to have hilar tuberculosis and vegetative endocarditis. For a period of 6 years prior to h death she had strongly positive Wassermann reaetions alternating wi negative reactions. Stokes has found that septic infeetions such as occu in patients with subacute bacterial endoearditis, as well as tuberculos may give isolated or repeatedly positive reactions for syphilis. Eagle (*2* observed a false positive reaction in pulmonary tubereulosis but attribute it to teehnical error beeause of the fact that the test was negative wh repeated 8 days later. Kilduffe and Hersohn (*57*) studied 200 serum obtained from patients with pulmonary tubereulosis by means of the Kolmer and Kline tests. Negative reactions to both tests were obtained wi 191 serums and positive reactions with 8 serums. Two of these were negative to the Kolmer test and gave a plus-minus and 2 plus reaction respetively to the Kline test. In all the remaining cases reacting positivel

corroboratory evidence in regard to the specificity was obtainable and nonspecific reactions did not occur.

Dünner and Mayer (*23*) carried out the Wassermann, the Meinicke clarification, the Kahn, and the Müller conglobation reactions on the blood serums obtained from 1,200 patients with pulmonary tuberculosis. Their study extended over a period of 1½ years. Of these 1,200 patients, 43 gave positive reactions to one or all of the tests, but they also had clinical signs of syphilis. There were 31 who gave positive reactions to one or several tests, and in these there was no history or clinical evidence of syphilis. Twelve of these came to autopsy, and in them no signs of syphilis were found. (Five with a history of syphilis came to autopsy, and in these also no signs of syphilitic change were found.) The authors conclude from this study that positive reactions for syphilis do occur in persons with pulmonary tuberculosis who have neither history, nor clinical or autopsy findings of syphilitic infection. Patients were observed in whom, with the advance of the tuberculous process originally negative, blood tests for syphilis became positive.

Infectious mononucleosis.—The etiology of acute infectious mononucleosis in man is unknown. Kolmer (*71*) states that whatever the cause may be, it is now well established that transitorily positive Wassermann reactions may occur in the disease in man, and these may be independent of the production of antibodies (agglutinins and hemolysins) for sheep erythrocytes. Kolmer carried out studies to determine whether or not Listerella monocytogenes could produce in rabbits the reagin or antibody-like substance responsible for the Wassermann and various flocculation reactions which occur in syphilis. He found that the intravenous immunization of rabbits with living and heat-killed avirulent strains did not produce complement-fixing or flocculating reagins for antigens commonly employed in the serum diagnosis of syphilis and did not produce agglutinin for sheep erythrocytes in the immunization of rabbits.

Wawersig (*128*) reported two cases of infectious mononucleosis with positive serologic reactions (Wassermann and Kahn) which returned to negative as the patients recovered. Among 60 cases of infectious mononucleosis which Bernstein (*4*) observed in a period of 5 years, serologic tests (complement fixation, Eagle flocculation, or both tests) were made in 37, and of these 6 (16 percent) gave positive reactions. In these 6 cases the Wassermann reaction became temporarily positive in 5, the Eagle test positive in 2, and doubtful in 2 others. The author points out that the Paul-Bunnell test may remain positive for 6 months or more and that the miscellaneous bacterial antibodies which not uncommonly appear in the blood of patients with this disease typically persist for many months, whereas the longest duration of a positive Wassermann reaction was 9 days and of the

Eagle reaction an even shorter period. Other cases are reported by Hat (*37*), Saphir (*111*), and Sadusk (*110*) who review the literature on thi subject. Saphir believes that infectious mononucleosis creates a disturb ance in the protein fractions of the serum, which renders the serum "labile" and may be responsible for a nonspecific protein reaction such as is see in pneumonia, malaria, and pregnancy.

Febrile diseases.—In the 1935 evaluation study the percentages of positiv results obtained in 46 cases of natural or induced fever were Hinton 2.3 an Kolmer 2.2. These were the only tests which gave positive results. Corri gan (*15*) studied the serums from 100 patients with febrile diseases and foun among them 3 which gave strongly positive Wassermann reactions. Tw of these were obtained in nonsyphilitic patients with pneumonia and i one of these the reaction became negative after the crisis; the other strongl positive reaction occurred in a nonsyphilitic patient with endocarditis. A weakly positive reaction occurred in a patient with epilepsy. The autho doubts the causal relationship of the temperature in producing the positiv reactions and states that since these nonspecific reactions in febrile con ditions occur so rarely they do not interfere with the serologic diagnosi of syphilis. Gunn (*36*) found occasional false positive reactions in patient with measles and chickenpox. He states that in the acute fevers there is a increase in the normal lipoidophile antibody content of the human serur or a physical or chemical alteration of its composition which permit complement deviation to occur even in the absence of syphilitic infection He points out that this change in the serum is present only for a short tim (from the 3d to the 21st day) and rarely persists into the fourth week Monticelli (*86*) performed 364 Wassermann tests (Frankfurt method) o the serums of 150 children with scarlet fever. The results were negative i all the cases. The author believes that the positive serologic reactions i scarlet fever which have been reported in the literature are caused by th sensitiveness of the antigens used. He advises that each country should hav an official method for doing the Wassermann reaction. Landau (7 studied the Wassermann, Kahn, and Sachs-Georgi reactions in the bloo obtained from 164 patients (mostly children) with scarlet fever. Th Wassermann reaction was positive in only 1 case (0.6 percent). Th patient also had positive flocculation reactions without having either his tory or clinical findings of syphilis. The Kahn reaction alone was positiv in 2 cases, becoming negative in 1 in the second week and being still pos tive in the other in the third week. (The tests were repeated after 2, 3, an 4 weeks). The Sachs-Georgi reaction alone was positive in 1 patien during the second week, becoming negative thereafter. The author con cludes that scarlet fever does not produce nonspecific Wassermann c flocculation reactions.

Some authors have reported the finding of positive reactions after injectio

of diphtheria serum in nonsyphilitic patients. Boas and Tölböll (*6*) examined 100 patients with diphtheria before and after the injection of antidiphtheria serum and found only 1 positive reaction which occurred 1 week after the serum treatment. This positive reaction became negative after 6 days. They concluded that an injection of diphtheria serum may occasionally bring about a positive reaction to a test for syphilis.

Whether or not certain other conditions may be responsible for false positive reactions has been a matter of debate in which the latest decision is that they do not produce nonspecific reactions. In this connection might be mentioned the following:

Jaundice.—The evaluation study of 1935 included tests on the serums from 51 cases of jaundice in which all the tests gave negative results. Davis and Sidel (*21*) found that 3 out of 102 records of patients with jaundice did not show evidence of a history or physical findings of syphilis and concluded that jaundice, in the absence of syphilis, does not cause false positive Wassermann reactions.

Malignancies.—In the evaluation study of 1935 the Hinton test gave 3.3 percent, the Eagle flocculation 1.7 percent, the Kolmer 1.6 percent of positive results. No positive results were obtained with the Kahn and the Kline tests. Eagle (*27*) elsewhere reports no positives in this group.

Pregnancy.—In the same evaluation study 54 cases of pregnancy were included. The Hinton test gave 1.9 percent of positive results; all the other tests gave negative reactions.

Spiegler (*117*), who found 0.45 percent of nonspecific reactions among 6,580 pregnant women, states that nonspecific reactions occur in pregnancy no more frequently than in the nonpregnant women or in the man.

Moore (*93*) states that serum treatment may produce false positive serologic reactions. He also points out that perhaps 1 person in 2,000 has a sufficient quantity of reagin or reagin-like substance in his blood serum to give a false positive reaction. This condition may be temporary or permanent. A false positive reaction should be suspected in a patient who in the absence of a history of syphilis or clinical evidence of the disease has a series of doubtful or weakly positive blood serologic reactions, conflicting results being obtained with different test procedures and in different laboratories. He outlines the study of this problem in the individual patient as follows: Careful history taking and careful physical examination, including blood smears for malaria parasites and for infectious mononucleosis. Repeat serologic tests for syphilis by several different technics, of which at least one is quantitatively titered. Low titer tests should be suspected of being false positives in young persons, who, if infected at all, may be presumed to have been recently infected and should therefore have high titer tests. False positives should be suspected when the reactions are negative with the more sensitive and positive with the less sensitive tech-

nics. Such reactions should be repeated in several different laboratorie of known dependability. False reactions should be suspected if the result are positive in one laboratory and negative in others. The patient' serum should be tested by complement fixation with spirochetal antigen and also with wholly nonspecific antigen, and false positives should b thought of if the serum reacts positively with all complement fixation tests If there are indications that a false positive has been obtained, prolonge serologic follow-up without antisyphilitic treatment is indicated. A good quantitative technic should be used, and those serums should be suspected which have markedly fluctuating or spontaneously falling titers. Member of the family and sexual contacts should be examined. The patient's cere brospinal fluid should be examined if a decision cannot be reached earlier Antisyphilitic treatment should be withheld until the diagnosis is settled.

Stokes and Ingraham (*122*) give the following outline of how to chec the report of a positive serologic reaction: (1) Inquiry into the source o the report. The report of a serologic reaction is worth only as much a the reliability of the laboratory and the responsibility and skill of th performer. (2) The time and circumstances of drawing the blood, includ ing particularly the presence of intercurrent infection (especially febrile) (3) No single positive report should ever be accepted without confirmation The test should be repeated in the same laboratory or in a different labo ratory, if done under sufficiently experienced direction. The performance o 2 or 3 standard test procedures may provide additional interpretativ evidence, but the difficulties of the interpretation increase with the numbe of tests and a corresponding degree of experience and expertness become desirable. (4) Clinical examination in the doubtful case must be searchin and conducted by one who is experienced in the recognition of individua relatively unfamiliar signs. They emphasize that the history of primar and secondary lesions taken as a routine has a margin of error rangin from 30 to 60 percent or even higher and is practically worthless in women

False Negative Reactions

A single negative reaction does not exclude the possibility of syphiliti infection being present, nor do repeatedly negative tests by every availabl procedure exclude this possibility. As Kolmer has pointed out, the test now in use give from 80.2 percent to 90.7 percent of positive reactions i the laboratories of their authors, and according to Moore (*91*) any tes which gives 80 percent or better of positive and doubtful results in know syphilitic patients may be regarded as satisfactory from the standpoint o sensitivity. However, as Kolmer states, there is no doubt that cases o symptomatic chronic syphilis and even of acute early syphilis as well a asymptomatic chronic syphilis may give false negative reactions by a methods now employed.

Aside from technical error, the second factor in the production of a negative Wassermann reaction in the presence of active syphilis is lack of sufficient reagin in the blood. This occurs, as Michael (*85*) has pointed out, in several stages of the disease. In rare instances it may be the result of lack of production of reagin even when spirochetes are abundantly present, as in malignant syphilis, or in the early weeks of life in congenital syphilis; oftener, however, it is due apparently to the small number of spirochetes present and to their being walled off by dense infiltration. The periods of the disease in which negative serologic reactions may be expected are early primary syphilis, late syphilis which is divided into (a) latent syphilis and (b) cases with sharply localized areas of activity (10 percent of cases with tertiary skin lesions), neurosyphilis (especially tabes with about 40 percent negative reactions), syphilis in early infancy, late congenital syphilis with active skin lesions, periostitis, interstitial keratitis, and certain cases under active treatment. There is therefore no justification for the disregard of the possibility of syphilis being present because a single negative or even a series of negative serologic reactions is obtained. A single negative reaction certainly does not absolutely eliminate the possibility of syphilitic infection. However, several negative reactions in the course of a routine study of a patient without history, signs, or symptoms of the disease may be considered as reasonably satisfactory evidence of the absence of syphilis.

If, in spite of the negative serologic reaction of the blood, the history or the physical findings of the patient are suggestive of syphilitic infection, the blood should be tested by several other serologic tests for syphilis; the provocative procedure and the serologic test series may be applied.

The Provocative Test

The provocative procedure is based on the principle that a small dose of an antisyphilitic drug, especially an arsenical, will activate a latent syphilitic infection and thus cause the production of an increased amount of syphilitic reagin which will be detected by a serologic test.

Belding (*2*) discusses the provocative test at length. He points out, on the basis of a review of the literature, that most investigators believe in the accuracy and value of the provocative test whereas a smaller number of them deny its value. They believe that all provocative reactions may be accounted for by variations in laboratory technic or in irrelevant changes in the serum of the patient. The technic of the provocative test varies with the different investigators in respect to the dosage and type of drug used, the time of taking the blood, and the method of performing the test. The dosage of arsphenamine varies from 0.15 gm. to 0.5 gm., the majority favoring a single dose of 0.3 gm. A single negative Wassermann reaction is usually obtained just previous to the administration of the drug, but a few careful workers demand a preliminary series of negative reactions. The time of

taking the succeeding tests appears to be largely a matter of persona opinion. Some investigators advise testing every day for 10 days, other on the 3d or 7th day, and still others at intervals up to the 42d day. Th provocative reaction may appear at any time within 3 weeks, although i is usually found between the 1st and 5th days.

The provocative procedure outlined by Stokes (*120*) consists of 7 dail Wassermann tests which are made following the intravenous injection o 0.3 gm. of arsphenamine, with daily observation of the patient. Th patient should be examined for flare-up of any visible lesions. Stoke states that this procedure is of value but should not be considered as a ultimate diagnostic criterion if it is negative. Belding states that a positiv provocative test is a sound procedure for the detection of a small amoun of syphilitic reagin but is in no way superior to a series of repeated Wasser mann tests.

In untreated syphilis the reagin content of the blood depends on th response of the patient and the course of the infection. In general th reagin content, with the exception of neurosyphilis, is roughly comparabl to the clinical progress of the disease. During the very early stages it i absent or present in only small amounts; it rapidly increases in amoun until it reaches a maximum during the late secondary or early tertiar stages and then gradually decreases as the disease becomes quiescent. A negative serologic reaction is found not infrequently in patients with clini cal syphilis and in patients without apparent active lesions but with definite history of syphilis of several years' standing.

There is a difference of opinion in regard to the daily fluctuation of reagi content. Belding (*3*) states that his observations on the titrated serums o syphilitic patients indicate that the fluctuations in the reagin content i old untreated cases over short periods of time are practically negligibl and that nearly all reported changes are the results of variation in the per formance of the test. He found uniform variation in the reaction of severa known serums on a particular day, discrepancies in reports on the sam serums between two laboratories, unaltered reagin content in patient examined over a period of several months, and gradual uniform reductio under treatment. However, changes from a strongly positive to a negativ reaction or vice versa sometimes unexpectedly occur with or withou treatment and are entirely distinct from the daily fluctuations.

Mohr and Smith (*87*) studied the daily variation of the reagin content o patients with late syphilis. These patients had either been on probatio for 1 year, after having received what was considered to be adequate treat ment, or they had been followed and treated intermittently for over years and were now receiving antisyphilitic treatment. In both group there was reason to believe that the syphilitic infection was quiescent.

A portion of the serum specimen of each individual patient was teste

on the day of collection by a quantitative complement fixation test, in which the minimum amount of serum giving a definitely positive result was determined. The remaining serum was frozen at —25° C. in order to minimize deterioration, until an adequate number of specimens was collected. The frozen specimens were thawed and tested on the same day with the same reagents by both quantitative Wassermann and flocculation technics. The Eagle modification of the Wassermann test was used. A titered Eagle microflocculation test was also used for the frozen serum specimens.

It was found that the titers of those serums tested in the routine laboratory at the time the bloods were collected varied to a surprising degree, while the titers of the accumulated specimens, kept frozen in the interim and tested simultaneously, were remarkably constant. The percentage-deviation of the individual serums from the average, when the serums were tested on the day of bleeding, varied from 0 to 162.5 percent with an average percentage-deviation of 55.4 percent. When the serums were accumulated and tested simultaneously, the average percentage-deviation fell to only 6.2 percent for the Eagle-Wassermann and 11.7 percent for the flocculation test.

It follows from this that the variations in serologic tests on the same patient are due primarily to variations in the sensitivity of the test and do not reflect changes in the reagin content of the serums. An evaluation of the therapeutic activity of drugs or treatment schedules based on the results of routine quantitative Wassermann determinations must be regarded skeptically. In view of the large variations encountered in day-to-day Wassermann titers, the rate of fall of reagin, to be of statistical significance, should be based on a large number of patients and at best would have a large probable error. Quantitative flocculation tests appear to be of greater value in such studies.

The authors further point out that this daily fluctuation in the sensitivity of the Wassermann test raises doubt as to the significance of the so-called provocative rise in serum reagin following the initial dose of an arsenical.

Barnett, Kulchar and Jones (*1*) have shown that small amounts of reagin are regularly present in nonsyphilitic serums as demonstrated with the Kline diagnostic test. Their definition of a unit of reagin is the least amount which will cause flocculation in the test. They determined the reagin titer of the serums of 32 adults without clinical or serologic evidence of syphilis before and 24 hours and 48 hours after the injection of 0.45 gm. of neoarsphenamine. None of the 32 serums contained more than 1 unit of reagin before the injection of neoarsphenamine. After 24 hours the reagin content had increased to 2 or more units in all but 5 of them. In 4 of the 5 a definite increase in reagin was found after 48 hours. In the fifth no increase occurred in the first 48 hours, but after 96 hours the reagin content was 3 units. In each of the 32 patients the reagin content of the serum increased after the

injection of neoarsphenamine to at least twice the original titer. Because of this regular increase in titer observed in nonsyphilitics, reagin was measured after the injection of neoarsphenamine in the serums of patients with treated syphilis who were negative to the usual Wassermann test. The majority had completed adequate treatment for early syphilis at least 1 year before. Although the mean values showed an increase in reagin content at both 24 and 48 hours, this was found to be much less uniform than in the nonsyphilitic patients. In 9 of 30 syphilitic patients no change in reagin content occurred, and in 21 there was an increase of 2 or more units. These authors conclude, on the basis of these findings, that the provocative reaction is an unreliable procedure and that a positive provocative reaction should not be considered as diagnostic of syphilis.

Craig and Nichols in 1911 reported that in 9 patients with syphilis and strongly positive Wassermann reactions the ingestion of 90 to 240 cc. of alcohol resulted in the finding of negative Wassermann reactions. Since then the effect of rendering a positive Wassermann negative has been attributed to the ingestion of alcohol. However, Brittingham and Rosen (*12*) who observed the effect of ingestion of alcohol on the results of the Wassermann, Kahn, and Hinton tests in 18 patients with untreated syphilis found alcohol to have no appreciable effect on these tests. The authors conclude that the effect of ingestion of alcohol on the Wassermann reaction has been overestimated and that the discrepancy between these results and many prevailing opinions is probably due to the greater sensitivity of modern serologic technic.

Another point of importance which should be emphasized in connection with negative serologic tests occurring in patients with syphilis or a history suggestive of syphilis is the fact that a negative blood test does not rule out involvement of the central nervous system. In other words, every person who has had a syphilitic infection should have an examination of the spinal fluid regardless of the finding of a negative blood reaction. In the Cooperative Clinical Group study (*100*) it was found that 26 percent of patients with negative blood reactions had asymptomatic neurosyphilis as evidenced by positive spinal fluid findings. This figure includes both early (30.9 percent) and late cases (22.6 percent).

Seroresistant Syphilis

The term "Wassermann-fast" has been applied to those patients who remain seropositive despite long and intensive treatment. Since such patients also have positive flocculation tests, Eagle (*27*) has recommended the use of the term "reagin-fast" instead, because it is the persistence of reagin which determines the positive serum reactions. Moore and Padget (*92*) use the expression "seroresistant syphilis," which is both logical and descriptive. They point out that there is no generally accepted definition

of seroresistance but that most observers agree that the concept should be based on an arbitrarily chosen span of time or amount of treatment and that a distinction should be drawn between patients with early syphilis and those who have had the disease for a long period of time. According to their definition, therefore, patients with early syphilis (infection of less than 2 years' duration) are considered to be seroresistant if the result of the serologic test for syphilis remains positive after 6 months of continuous treatment, and patients who have had the infection for more than 2 years are said to have seroresistance if the serologic test for syphilis is positive after the equivalent of a year of treatment. The number of syphilitic patients with seroresistance is in direct proportion to the sensitivity of the serologic test which is used. As has already been pointed out, Barnett, Kulchar and Jones have found by use of the Kline diagnostic test that even nonsyphilitic serums contain small amounts of reagin.

The cause of seroresistance is unknown, but two theories have been suggested to explain it. The first of these is that seroresistance indicates persistent foci of spirochetes or progressive syphilitic lesions. The other theory is that the persistence of reagin in the circulating blood following antisyphilitic therapy is only a manifestation of persistent immunity. Moore and Padget state that on the basis of present knowledge seroresistance in cases of early syphilis must be regarded as a manifestation of persistent foci of spirochetes or progressive activity of the disease. In cases of late syphilis, however, seroresistance may result entirely from the persistence of well-established immunity. In early syphilis two factors are of extreme importance in determining the incidence of seroresistance; first the system of treatment employed and second, the presence or absence of involvement of the central nervous system. Among the patients studied by Moore and Padget only 11 percent of patients who received continuous treatment for early syphilis were seroresistant, whereas 37 percent of those treated intermittently and 68 percent of those whose treatment was irregular had positive reactions to serologic tests more than 6 months after treatment was begun. All other factors being disregarded, they found seroresistance in only one-sixth of the patients whose cerebrospinal fluid was normal or fell into group I–a (6 cells or more with all other findings normal), but it occurred in almost one-fourth of those whose spinal fluid was of group I–b (5 cells or more with protein increased) and in almost half of those manifesting changes typical of group II (positive complement fixation or flocculation tests with larger amounts of spinal fluid, the results of the other tests being variable) or group III (the paretic formula).

The Cooperative Clinical Group study (*100*) showed that of 31 patients who were seroresistant after having received adequate treatment for early syphilis, 74 percent had positive spinal fluid reactions. Of 193 patients who were seroresistant after having received adequate treatment for late

syphilis, 75 percent had positive spinal fluid reactions. Of 105 patients adequately treated for early syphilis whose blood reactions had become negative, 17.1 percent had a positive spinal fluid, whereas of 137 patients adequately treated for late syphilis whose blood reactions had reversed to negative, 41.6 percent had a positive spinal fluid reaction. In late latent syphilis seroresistance is so common that it cannot be considered to be presumptive evidence of involvement of the central nervous system.

Lord (*76*) in 1928 reviewed the histories of all patients treated in the syphilis clinic of the Johns Hopkins Hospital between October 1918 and January 1927. Of 8,500 patients who were seen during this period, 900 received regular treatment for a year or more. In the latter group there were 118 who fulfilled the arbitrary criterion of seroresistance in that they had persistently positive tests after having received 1 year of regular, continuous treatment. These patients had had a careful physical examination and spinal fluid and roentgenologic examinations. The study of these cases showed that sex was of no significance and that age of the patient was important only in relation to the chronicity of the disease. Seroresistance was found to be most common in patients with neurosyphilis (31 patients) and next, in the order of frequency, in cardiovascular (21 patients) and bone syphilis (13 patients). In this group of 118 patients proof of active syphilitic infection could be found in 47.5 percent; in 49 percent the activity of syphilis could not be definitely determined; only 3.5 percent were considered clinically well. Lord concluded that seroresistance cannot be said to be without significance because of the absence of demonstrable lesions and that it should be accepted as indicating the possibility that relapse will occur at some indeterminate time in the future.

Among 1,200 patients treated for syphilis which were reported by Wheeler (*129*), there were 300 who were seroresistant as determined by the Hinton test (166 of these also had positive Wassermann tests); 200 of these were carefully studied. Among these 200, there were 192 who were found to have definite syphilitic involvement of one or more organs. Cardiovascular syphilis was present in 65 patients, neurosyphilis in 24, splenohepatic lesions in 22, congenital syphilis in 13, syphilis of the bones in 4, and syphilis of the eye in 2. Many of the patients in this group had bad habits of living and coincident nonsyphilitic diseases, which may play a contributory role in producing a seroresistant condition. Only 8 of the 200 patients had no complaints or any clinical evidence of organic involvement, the persistently positive serum reaction being the only evidence of syphilis. Wheeler concludes that organic syphilitic involvement is in most instances the cause of persistently positive serum reactions and that such reactions usually indicate uncured syphilis.

O'Leary (*99*) in discussing seroresistant syphilis states that a persistently positive blood test is encountered in early syphilis in cases in which treat-

ment has been inadequate, in cases in which the patient is a "chronic relapser" who has recurrent lesions of the mucous membrane and skin, in cases which have a positive spinal fluid, and in those in which visceral syphilis has developed as a complication of early syphilis. It is difficult to state the exact amount of treatment which may be termed "adequate" in an individual case of early syphilis, to foresee the amount of treatment which will assure a permanently negative blood test. In some cases the serologic reaction of the blood will remain negative after a few injections of arsphenamine while in others 50 or more injections are necessary to produce such serologic negativity. Not only is sufficient treatment necessary but also regularity in its administration and sufficiently large doses of arsphenamine. However, doses exceeding the tolerance of the particular patient should not be given since complications of treatment such as dermatitis, neuritis, and jaundice are more numerous among those who receive large doses, and since the development of these treatment-complications may prevent the continued administration of the drug to which the patient has developed the intolerance, but which he needs if his infection is to be cured. Sometimes a change in the type of drug used, for example from neoarsphenamine to arsphenamine, may result in serologic reversal.

Moore and Padget, in discussing the significance of seroresistance, report that they found among patients with early syphilis who had received adequate antisyphilitic therapy that 23 percent of the seroresistant group, but only 5 percent of the patients who showed prompt serologic reversal, had infectious relapse. Neurosyphilis occurred in 31 percent of the former but in only 18 percent of the latter. In late latent syphilis, however, the incidence of progression or relapse was essentially the same among patients who were seroresistant and those who had negative blood reactions. In patients with other forms of late syphilis, especially cardiovascular syphilis or neurosyphilis, seroresistance is so common that special interpretation was impossible. Wile (*130*) points out that in such cases, even if serologic reversal is brought about, this reversal would not necessarily indicate that the patient had been cured. Wile is of the opinion that many patients with seroresistance, especially the late latent cases, are injured rather than helped by the excessive amount of treatment to which they are only too often subjected by the physician who is determined to get a negative serologic reaction, regardless of anything else.

In the management of seroresistant syphilis a differentiation must, of course, be made between early and late syphilis. Every seroresistant patient with early syphilis should immediately have an examination of his spinal fluid because this finding is so frequently associated with involvement of the central nervous system. If the cerebrospinal fluid is normal, further continuous intensive treatment will result in serologic reversal

almost uniformly within a year. The same treatment system should be continued for a full year after serologic reversal has occurred.

In patients with late latent syphilis the cerebrospinal fluid should also be examined, and repeated, careful clinical and roentgenologic search made for syphilitic involvement, particularly of the cardiovascular, skeletal, and central nervous systems. If syphilitic lesions are found, treatment is planned according to the system of the body which is involved. If, however, careful study discloses no demonstrable changes which can be attributed to syphilis, the patient is considered to have late latent syphilis and should receive the treatment recommended for late latent syphilis, no additional effort being made to bring about serologic reversal. The employment of special measures for the treatment of such patients is considered to be neither necessary nor desirable. "High pressure" intensification of treatment by the use of unusually large dosage, short intervals, or by nonspecific methods is not necessary because it subjects the patient to an increased risk without the certainty of a better prognosis. Every person who has had a syphilitic infection should have periodic observations, both clinical and serologic, for the rest of his life.

PRESUMPTIVE TESTS

Stokes (*121*) sounds a note of warning on the use of presumptive tests and the tendency to discard the complement fixation reaction. To quote him.

> Serodiagnostic service, critically important to the uncovering mechanism as it is, for the moment is suffering from that most unfortunate influence, the economy squeeze. The disposition to do away with complement fixation and throw out the animals, and at the same time to make a high positive showing on tested bloods as a demonstration of efficiency (frankly so expressed in several letters from health and laboratory authorities which I have received), is leading to what I believe is a mistaken adoption of the so-called exclusion tests as first-line procedures. From what I have seen, I agree with Eagle in questioning whether the ultrasensitive procedure really shows anything trustworthy that the adequately performed original test could not have supplied. The disposition to boost the showing of positives in the work of a serologic laboratory by the selection of supersensitive first-line tests is, too, a regrettable form of bias in a procedure which at best can never wholly escape interpretative personal equation. I accept a standard diagnostic precipitation, as distinguished from complement fixation, test (and for this country the Kahn, Kline, Eagle, and Hinton tests are acceptable as standards) as a proper first-line test. But the reexamination of doubtfuls and questioned positives or negatives, I still thoroughly believe should include a complement fixation procedure, preferably the Kolmer. Partial positives (except in treated cases) are not diagnostic, but rather interpretative and investigative material for specialists, and whether reported in titer or in pluses, with or without the results of repetitions, should be distinctly understood to be of only limited significance. They should be referred to an experienced or even syphilologic evaluator for interpretation, if possible, and are dangerous sources of error when reported for diagnosis to the average doctor.

An editorial (*28*) in the Journal of the American Medical Association also points out pitfalls in the application of presumptive tests to the serodiagnosis

of syphilis. In reference to the claims made for the presumptive tests that they are so sensitive that a negative result "excludes" syphilitic infection while a positive result is "presumptive" evidence of syphilis, it is pointed out that not merely does no laboratory test yet devised "exclude" syphilis, but no laboratory test even excludes the presence of serum reagin. Furthermore it is not necessarily true that a serum giving a negative Kline exclusion or Kahn presumptive result will be negative by every other technic used. In any extended series of tests, certain syphilitic serums are detected only by an ordinarily less sensitive procedure. These paradoxic results are particularly common when both a flocculation and a complement fixation test are used. The flocculation phenomenon is peculiarly susceptible to zone reactions, i. e., false negative results caused by the presence of excessive amounts of reagin. A serum may be negative with any flocculation test, screen tests included, when tested as a whole serum, yet the complement fixation test may be clearly positive and the flocculation procedure may be similarly positive if the serum is tested in 1:10 or 1:20 dilutions. For these several reasons, it is pointed out that the term "exclusion" test is misleading. It is advised that these procedures be referred to as "screen" tests.

A more important criticism is made relative to the manner in which these tests are used. It is pointed out that although the originators of these tests did not intend them to be used for diagnostic purposes, reports as difficult to evaluate as "exclusion test positive, diagnostic test doubtful" are presented without explanation to physicians and thus invite the possible mistaken diagnosis of syphilis. It has been found that in the average laboratory these tests show from 1 to 10 percent of false positive reactions. Therefore when a laboratory obtains a positive "exclusion" or presumptive result, the burden of proof rests on the laboratory that such a result is not due to laboratory error but reflects the actual presence of reagin.

It should be insisted upon that the clinician is not informed of the result of a hypersensitive screen test unless it is negative, because the weeding out of negative serums is its only proper function. After a positive or doubtful screen test is checked by one or more specific diagnostic tests, only the results of the latter tests should be reported by the laboratory and the result of the "exclusion" or "presumptive" test should be withheld. When used solely as an intralaboratory procedure to facilitate the recognition of negative serums, the hypersensitive screen test may fill a useful function, but to report positive or doubtful screen tests to the physician as quasidiagnostic tests which he must weigh and interpret cannot fail to cause confusion and invite the mistaken diagnosis of syphilis.

Moore (*91*) advises that the use of the presumptive and exclusion tests be limited to three sets of circumstances: (1) In the serologic testing of donors for blood transfusion, as an added safeguard for the prevention of transfusion syphilis, (2) in syphilis clinics in which there is expert clinical

interpretation, and (3) in following the results of treatment in patients definitely proved to have syphilis. He says that in the absence of such limitations, the clinician who is served by a laboratory which employs one of them as a routine diagnostic measure must be prepared to accept a risk, ranging from 2 to nearly 9 percent, of false nonspecific results in nonsyphilitic patients.

Gould (*33*) points out that the Kline exclusion test is not a screen test in the sense that it excludes all blood specimens which give positive reactions to other satisfactorily specific serologic tests. He reports one instance in which the Kline exclusion test was negative but in which the Kolmer test was strongly positive. These results were verified by repeat tests on the same blood specimen. There were two other scrums which gave doubtful reactions with the Eagle complement fixation test and negative Kline exclusion reactions. It seems for this reason that even the term "screen test" is not quite suitable but probably is the best term available at present, providing its limitations are kept in mind.

COMPARATIVE EVALUATION OF SERODIAGNOSTIC TESTS

Since the ideal serologic test which meets the requirements of absolute specificity combined with a very high degree of sensitivity, has not as yet been devised, the value of the tests available is only relative as determined by comparing the different tests with one another. The methods used for such comparisons have been the following:

(1) The comparison, by the originator of a test, of his test with one or several other tests. This method has the disadvantage that the originator of one test will give primary attention to the careful execution of his test and will prepare the ingredients for the other test or tests and carry out the performace of this test or tests less efficiently than in the case of the test which he has devised. This may be due to one or both of two factors. Either he is less interested in the other test or he is less efficient in performing it, or both. For this reason his own test may give much better results than the test with which he is comparing it, whereas in the hands of its originator the other test may show up much better, for the same reasons indicated. In the comparisons of definite flocculation reactions with complement fixation reactions, the difficulty too often has been that the flocculation test in question was compared with the "Wassermann reaction" whose technic is not given. The "Wassermann reaction" may therefore have been an antiquated procedure which could not be compared with a highly specific and sensitive complement fixation test such as the Kolmer, and a favorable showing of the test in question on comparison with an outmoded Wassermann procedure tells exactly nothing about the relative efficiency of this new test.

(2) The comparison of tests in various laboratories. It would seem that the conditions here would be better for obtaining unbiased results. Nevertheless the same factors apply, and the results are further influenced by the general efficiency of the laboratory which may be very low.

(3) A comparison of the results published by the various originators of tests which they have obtained with their own tests. In this all the tests are apt to make a very good showing because of the fact that each of the originators is interested in his own test and will be lenient in his interpretations. It is as yet impossible to make these tests completely objective, and a certain amount of subjective interpretation cannot be avoided.

(4) A comparison of tests made on samples of the same serums by the various originators of tests to whom these samples represent unknowns. Such comparisons have been made at the serologic conferences sponsored by the League of Nations and later by the United States Public Health Service in cooperation with the American Society of Clinical Pathologists.

(5) Comparisons have also been made of the results obtained on the same specimens which were tested simultaneously by the originators of methods and by various State laboratories. The purpose of such comparisons has, however, been primarily to study the efficiency of the laboratories in the performance of these tests, and the tests as done by the originators in their own laboratories served as controls.

The Committee on the Evaluation of Serodiagnostic Tests for Syphilis in the United States (*113*) made a thorough analysis of the factors concerned in the comparative evaluation of serologic tests. Kahn is quoted as saying that "authors of methods are no less human than others, and they are likely to magnify the merits of their respective methods. The result is that clinicians will often hear diametrically opposed views as to the value of a given method, making it difficult for them to decide on the method of choice." There is no definite criterion for evaluation since there is difference of opinion as to the relative values to be given to sensitivity and specificity in determining the comparative value of different tests. The Committee also pointed out that a study of many of the numerous reports in the literature reveals the lack of conclusiveness in individual studies. They may involve series of cases in which the syphilitic and nonsyphilitic subjects are carefully selected, so that a higher proportion of positive reactions for any test is indicative of greater sensitivity or may deal with less carefully analyzed material where the element of false positive reactions might account for at least part of an apparently greater sensitivity. In some articles the cases of syphilis tested are classified according to the stage of the disease, while in others they are not so divided. The greatest variations usually occur between the results obtained by the originator of a method when he compares the findings with his tests and with other methods, and those obtained with the same tests when carried out in another laboratory.

Keim and Kahn (*53*) in 1924 studied a series of 2,500 cases which were clinically free from syphilis by means of the Kahn test. Negative reactions were obtained in 2,493 cases; 1-plus reactions were obtained in 4 cases, 2-plus reactions in 2 cases, and a 3-plus reaction in 1 case. These results indicate that the Kahn test possesses a high degree of specificity for syphilis (99.7 percent).

In another study by the same authors (*54*) of 2,600 cases "Wassermann" and Kahn tests were carried out simultaneously. The statement is made that both an ordinary antigen and a cholesterinized antigen were used in the Wassermann test. It was found that there was agreement among the 3 tests in practically 90 percent of the cases of primary syphilis examined. There was complete agreement in practically all of the cases of secondary syphilis. In tertiary syphilis the Kahn test was found to be somewhat more sensitive in bone, skin, and mucous membrane involvement. The "long ice box fixation Wassermann test" was slightly more sensitive in visceral syphilis and also in syphilis of the central nervous system. In latent syphilis the results obtained with the two tests were comparable. The Kahn test was found to be slightly more sensitive than the "sensitive Wassermann reaction" in congenital syphilis. Among 1,975 nonsyphilitic control cases the Kahn test gave two 1-plus reactions and two 2-plus reactions.

In 1927 Kolmer (*64*) published a comparison of the Kolmer tests as conducted in his laboratory and the Kahn tests as conducted in Kahn's laboratory which showed the following:

	Cases	Kolmer positive	Kahn positive
		Percent	*Percent*
Primary syphilis	24	67	58
Secondary syphilis	6	100	100
Tertiary syphilis	24	71	54
Neurosyphilis	20	70	66
Congenital syphilis	30	40	37
Treated syphilis	105	44	47

Kolmer (*65*) in 1928 reported that the percentage of agreement between the Kahn test and the Kolmer test is approximately 94 to 96 under routine conditions. He stated that the Kolmer test is generally more sensitive in untreated syphilis, but the Kahn test is slightly more sensitive in some cases of treated syphilis. The sensitivity and specificity of the Kahn reaction is influenced by the time when the readings are made. He pointed out that the Kahn reaction is subject to as much variation in different laboratories as the complement fixation reaction.

McIntyre and Gilman (*87*) made a clinical comparison of the Kolmer test and the Kahn test in syphilitic cases. This study was pointed out by

Kolmer as being a valuable one and for that reason is reviewed here. Altogether 1,767 tests were studied of which 1,394 were performed on serums from cases of proved syphilis. The remaining 373 were serums of patients with various types of skin diseases and of persons in whom a study for the possible presence of syphilis was made and was found to be negative. A clinical diagnosis of syphilis was based on a complete general physical examination and history, special examinations when indicated, serologic follow-up of the blood and spinal fluid, and family investigations in many instances. In proved syphilis the agreement between the two tests was 83.3 percent and the disagreement was 16.7 percent. In all types of syphilis the Kolmer test gave a higher percentage of positive reactions except in visceral syphilis, in which the two tests were equal. The total percentage of positive reactions of the Kolmer test was 62.4 while the Kahn test gave 53.3 percent positive reactions. When slightly positive reactions were included, the total percentage of positive reactions for the Kolmer test was 68.3 and for the Kahn test, 70.5. The percentage of absolute negative reactions for the Kolmer test was 31.7 and for the Kahn test, 29.5. These percentages are for both treated and untreated syphilis. In proved non-syphilitic cases the percentage agreement between the two tests was 96.7 and the disagreement 3.3.

In 1932 Kolmer (*66*) reported on a comparative study of the Kolmer test with the Kline and the Kahn tests. He stated that the reactions agreed in 86.7 percent of more than 1,000 serums and disagreed in 13.3 percent. He found the Kline test to be more sensitive than the Kahn and Kolmer tests, but it gave a higher percentage of false positive reactions than the Kahn test whereas the Kolmer test gave no false positive reactions in this series.

Kline (*59*) in 1926 published the results of 2,800 Kline tests for syphilis with clinical and serologic comparisons. The Kline test was found to agree with the condition of the patient in 94.9 percent of 2,809 tests which, he states, is practically the same amount of agreement as that of "a sensitive Wassermann test" and the Kahn test. It was found to agree or relatively to agree with "one Wassermann test" in 92.5 percent of 2,375 tests, with "another Wassermann test" in 90.5 percent, and with the Kahn test in 95.9 percent of tests. Rarely were negative Kline tests obtained in syphilitic serums which gave a positive Wassermann reaction. As a rule, the Kline test was found to be more sensitive than the "Wassermann test" early in syphilis and in cases of treated syphilis.

Under the direction of Hinton, Cheever and Splaine (*13*) made a comparison between the Hinton, the Kahn, the Kline, and "the Wassermann" tests. (For the "Wassermann test" both guinea pig heart and human heart antigens were used.) Altogether 1,610 cases were studied both clinically and serologically. It was found that 260 cases showed discrepant reactions among which the Hinton test showed the largest number of

positives in the known syphilitics and as few false positives in the non-syphilitics as any of the other methods. They state that in primary syphilis the value of the Hinton test was found to be only slightly better than "the Wassermann test." They further state that in the largest group of this series, that of asymptomatic syphilis, where one must be guided either by serologic tests or a less certain factor, namely judgment, they feel that the demonstrated increase of 50 percent in sensitiveness makes the Hinton test a superior one, and they are convinced that the Hinton reaction is a safer criterion of cure than a negative Wassermann reaction.

Eagle (*24*) in 1933 reported on a clinical and statistical evaluation of the Eagle flocculation test. This was based on the comparison of the Eagle and Wassermann reactions in 26,611 serums, and of the Eagle and Kahn reactions in 2,473 serums. The sensitivity of the tests was evaluated on the basis of 10,383 tests on the serums of known syphilitics. It was found that between 72 percent and 75 percent of the serums of these patients gave positive or doubtful Eagle reactions as compared with 58.7 percent with the Wassermann (Eagle's complement fixation test) and 60.2 percent with the Kahn test. The remaining 16,228 tests were made on 14,000 patients in other dispensaries and in the general hospital. The author states that one of the points of superiority of the Eagle flocculation test is the comparatively small incidence of doubtful results. In the total series of tests 1 out of every 26 was Wassermann or Kahn doubtful, while only 1 in every 107 gave a doubtful Eagle reaction.

Boerner, Lukens and Gilman (*11*), working in Kolmer's laboratory, reported in 1936 on a study of the relative sensitivity and specificity of the Kolmer, Kahn, and Eagle flocculation tests. Tests for sensitivity were carried out on patients under study or treatment in the syphilis clinic or syphilitic patients coming from other services. Tests for specificity were based on a study of a series of selected normal persons, considered non-syphilitic on the basis of past history and social status. The results obtained on 2,730 patients studied were: (1) All tests negative in 1,884; (2) all tests positive in 483; (3) serologic discord, i. e., one or more tests negative or doubtful in 163—the majority of these cases came from the syphilis clinic and represented cases under treatment; (4) all tests negative in 200 certainly nonsyphilitic persons—this group represented the control and was used to confirm the specificity of all three tests. As a single test the Eagle (96.1 percent positive) exceeded the Kolmer (84.5 percent positive) and the Kahn (82.1 percent positive). A combination of all three tests gave the greatest number of positive reactions. The showing of the Kolmer and Eagle tests combined (97 percent positive) exceeded the usually duplicated tests, namely, the Kolmer and Kahn (88 percent positive), and gave 1.2 percent more positives than the Eagle and Kahn combination. In regard to relative specificity, the Kolmer and Kahn applied to 200 certainly non-

syphilitic serums gave 100 percent negative results, while the Eagle test gave 1 doubtful and 99.5 percent negative reactions. None of the three tests gave false positive reactions. The false doubtful reaction obtained with the Eagle test was repeated with the same result, thus eliminating the possibility of technical error.

Davies (*18*) applied the micro-Hinton and the capillary Hinton tests to the study of 372 serums obtained at the Infants and Children's Hospital in Boston. These Hinton tests were controlled by clinical diagnosis, the regular Hinton test, and "the Wassermann test." The reactions agreed with the clinical picture in all but 11 cases; 5 of these were false positive reactions, 5 false doubtful, and 1 false negative. In other words there were nearly 3 percent of nonspecific reactions. Four of these nonspecific reactions are said to have occurred in febrile children, but the cause of their fever is not explained. One false positive occurred in a case of rat-bite fever. The false doubtful reactions are not explained. These modifications of the Hinton test cannot on the basis of these findings be said to be highly specific in the hands of their author.

That Hinton is probably using an inferior modification of the complement fixation reaction in his comparative evaluations of the Hinton test is suggested by his publications in which he severely criticizes "the Wassermann test" for lack of sensitiveness, lack of specificity, and lack of consistency, and in which he states that "the Wassermann test" fails in 50 percent of cases of primary syphilis, in a few cases of secondary syphilis, and in from 40 to 60 percent of tertiary syphilis (*45*). He apparently has not used the Kolmer test because it is not mentioned in any of the comparative studies carried out by him and his coworkers.

DISCREPANCIES AMONG THE RESULTS OF DIFFERENT TESTS

A puzzling and unexplained phenomenon in serologic examination is the discrepancy in results obtained with different tests on the same serum. The Kolmer test, for example, might be completely positive and the Kahn or some other precipitation test negative on the same serum, or vice versa (*34*). Such discrepancies occur most frequently in treated cases although, as Levine (*75*) has pointed out as being his experience, consistently positive complement fixation results may be obtained in some instances of early syphilis in which the flocculation test was not yet positive. The reactions in the same patient may also show fluctuations from day to day, in the absence of treatment. Greenbaum and Yagle (*35*) examined the serums of 50 untreated syphilitic patients on 12 consecutive days by means of the Kolmer and Kahn tests. They found that 42 gave uniform reactions to both tests with only slight variations throughout the series. In the remaining 8, variations occurred in 1 or the other of the tests. These variations went from one extreme to the other, but it was found that one or the other

test almost invariably caught up any failure in either to detect syphilis. In only 2 of the 8 instances in which wide variations occurred were both tests negative on the same day during the series. They point out that this demonstrated the value of performing both Kolmer and Kahn tests on every serum examined. They noted that variations occurred with both of these tests and thought that this is undoubtedly indicative of a change from day to day in the reagin content of the blood. But when it is considered that one test may be completely positive and the other completely negative on the same serum on the same day and consideration is given to the assumption that each of the tests is an indicator of the reagin present, satisfactory explanation is not quite so simple. Variations are also undoubtedly due to technical factors.

Crawford and Ray (*16*) report on a comparison of the Hinton test with the Wassermann test at Massachusetts General Hospital in a series of cases in which the Hinton reaction was positive and the Wassermann reaction negative. Since the Wassermann test used was stated to have been "a modification of the original Wassermann test" without explanation of its technic, such a study is worthless from the reader's point of view. The outstanding and rather surprising result of this study was, however, the large number of false positive reactions (positive Hinton reactions unconfirmed by subsequent Hinton tests in patients with no history or clinical findings of syphilis) obtained with the Hinton test, namely, 48 out of a total of 335 cases (13.7 percent). The authors state that this finding implies that the Hinton test, as done in the laboratory of the Massachusetts General Hospital is lacking in specificity.

The Kline, Eagle flocculation, and Kolmer tests were applied to the study of 3,000 serums by Pierce, Patterson, Stevenson and Torbert (*104*). They found all 3 tests to be negative in 2,355 serums and positive in 353 serums. Discrepant results were obtained in 292 serums. These were divided into 2 classes, one in which the disagreement persisted as long as the testing was continued and one in which the disagreement finally disappeared in the direction of positive or negative. It was possible to prove that 254 of these specimens were from patients who actually had syphilis, which included early primary, central nervous system and congenital syphilis, and treated cases. In 22 of the cases of this group showing discrepancies in serologic reactions no evidence of syphilis could be found, and these tests, with one exception, finally became negative. They were therefore considered to be false positive reactions. The authors conclude that these data clearly demonstrate that the use of several serologic test methods definitely increases accuracy and materially lessens the danger of reporting false positive results. They advise that the Kolmer be one of the tests used because it is less sensitive than the Kline and Eagle flocculation tests but is very specific and therefore is a check against false positive results.

Kilduffe (*58*) in 1931 tested 2,623 serums with both the Kolmer and Kline methods. He found that 2,115 (80 percent) were negative to both tests, 2,192 (83 percent) were negative to the Kolmer, and 2,212 (84 percent) were negative to the Kline test; 383 (14 percent) were positive to the Kolmer and 462 (16 percent) were positive to the Kline test. While the Kline test gave 79 more positive reactions than the Kolmer test, 45 (57 percent) of these were plus-minus reactions which in the absence of definite knowledge of syphilis in the patients in question had to be regarded as without diagnostic significance. In 252 of the positive reactions both tests agreed but the degree of positivity varied. The author often observed that a serum on a single test might be positive to one and negative to the other procedure or vice versa, which fact emphasizes the value of their coincident use.

OFFICAL EVALUATION STUDIES

Health Organization, League of Nations

The first serologic laboratory conference was held in 1923 in Copenhagen (*107*) under the auspices of the Health Organization of the League of Nations. The United States was not represented at this conference. Various modifications of the Wassermann reaction were found to be more sensitive than the flocculation reactions and gave no or very few nonspecific reactions. The serologists who used several antigens obtained results which were no better than those who used only one antigen. The use of active serum was found to increase sensitivity but at the expense of specificity. It was decided that the flocculation reactions could not replace the Wassermann test, but it was found that they frequently gave positive results in patients with syphilis, in whom the Wassermann reaction was negative. It was observed that slight variations from the technic suggested by the originators of methods seriously affected the results. It was therefore strongly advised to follow closely the directions of the author in carrying out the tests.

The second serologic laboratory conference was held in 1928 in Copenhagen and was also sponsored by the Health Organization of the League of Nations (*49*, *82*, *96*, *108*, *109*). Fifteen serologists took part; 7 of them performed various modifications of the Wassermann reaction, and 8 performed flocculation reactions which included the Meinicke opacification reaction, the Müller conglobation reaction, the Murata reaction, the Sachs-Georgi (lentochol) reaction, the citochol reaction, the sigma reaction, the Vernes reaction, and the Kahn reaction. A total of 944 blood samples were examined of which 502 were from syphilitics and 442 from nonsyphilitics. Kahn was the only serologist representing the United States. Since he performed only his own test, which is a flocculation reaction, the United States was not represented at the conference as far as the complement fixation

test for syphilis is concerned. The Kahn test was done by both Kahn and Boas (Copenhagen).

Something apparently went wrong with the Wassermann reactions as they were done at this conference. Most of them gave so many nonspecific results that they could not be considered to have any practical value. The only Wassermann modification which gave no nonspecific reactions was that of Harrison and Wyler which had a sensitivity of only 41.8 percent, as compared with a sensitivity of 63.5 percent of the Müller conglobation reaction (with 0.2 percent of nonspecific reactions) and with a sensitivity of 61.1 percent of the Kahn test as done by Kahn (with no nonspecific reactions). The Kahn test as performed by Kahn gave 1.12 percent, the Kahn test as performed by Boas, 1.38 percent, and the Müller test, 2.31 percent of false doubtful reactions. Sachs (*109*) points out that it would be totally incorrect to conclude that the unsatisfactory results obtained with the Wassermann reactions at this conference are shortcomings of the Wassermann test itself. He and other participants at the conference attribute them to changes in external conditions which can more easily affect the complicated system of the Wassermann than that of the flocculation reactions—the complement used, the performance of the tests, or the time factor. He feels that there must have been some source of error if one compares the results obtained with the very favorable results of the Wassermann reactions at the 1923 Copenhagen conference. The conclusions which he draws are that a number of flocculation reactions are at least comparable to the Wassermann reaction and that at the 1928 Copenhagen conference they were superior to the Wassermann reaction.

Of the flocculation reactions the most sensitive were found to be the Müller conglobation and the Kahn.

Sachs points out the difference in the results obtained by Boas and by Kahn with the Kahn test. Boas obtained only 58.5 percent sensitivity with 0.7 percent of nonspecific reactions. There was not only a quantitative but also a qualitative difference in the results obtained by these two serologists. This qualitative difference is shown by the fact that there were direct inversions in the results obtained by Kahn and Boas, in that some reacted more strongly to the Kahn test or were positive only to the Kahn test as done by Kahn, and the others were just the reverse. The individual factor apparently, therefore, plays a not inconsiderable role in the execution and reading of the Kahn test.

Doubtful reactions were interpreted as being negative. The Kahn test as done by Kahn had fewer doubtful reactions among nonsyphilitics (1.1 percent) than the Müller conglobation reaction (2.3 percent).

An important question which was discussed at this conference was whether the Wassermann is no longer necessary in the serodiagnosis of syphilis.

The Copenhagen conference has strongly advised that at least two different serologic methods should be used for the serum diagnosis of syphilis. A large number of the participants at the conference, among them most of the originators of flocculation reactions, have recommended that the Wassermann reaction be one of the two tests used. This was based on the viewpoint that theoretically many serums would react positively only to the Wassermann and not to flocculation reactions, that complement fixation and flocculation supplement each other, and that the evaluation of a weak or doubtful flocculation reaction is supported by a strongly positive Wassermann reaction, and vice versa. The material of the Copenhagen conference offered examples of this, even though 2 flocculation reactions were extremely sensitive at this conference. Sachs points out that the apparent equal value of serologic reactions by no means indicates congruence, so that one procedure completely replaces another. Even when two methods give the same percentage of positive reactions with syphilitics and are comparable in regard to nonspecific reactions, the positive reactions in syphilitics obtained with the two tests do not necessarily affect the same serum samples. As a matter of fact, that such divergences occur is an experience which, in spite of all increases in sensitivity, has been confirmed, and the results of the Copenhagen conference support it. Not only was this shown by cases in which the flocculation reactions were negative and the complement fixation reaction was positive, but also by the fact that the reactions which were found to be the most sensitive, namely, the Müller conglobation reaction and the Kahn reaction, by no means gave identical results. In many cases only the Müller and in many others only the Kahn reaction were positive. The most sensitive procedure with the most sensitive technic does not pick up all blood samples which will react positively with a less sensitive test. The conclusion of the conference was therefore that the maximal diagnostic value lies in the simultaneous use of several different procedures. The conference did not make any statement in regard to the relative value of the different flocculation tests.

As has already been pointed out above, the majority of originators of flocculation tests who took part in the Copenhagen conference in 1928 have advised that the Wassermann reaction be one of the tests used simultaneously in the serum diagnosis of syphilis. The only originator of a method, including originators of flocculation tests, who has published an opinion to the contrary is Kahn, the originator of the Kahn flocculation test and the representative at the conference of the United States, the country whose complement fixation tests were not represented and could therefore not demonstrate their worth. Kahn (*49*) states that he does not concur in the view held by the conference that theoretical and practical considerations make it advisable that the Wassermann reaction should be one of the tests

used simultaneously in the serum diagnosis of syphilis. He is of the opinion, in spite of the evidence presented, that his flocculation test is the only test needed.

Of 122 spinal fluids that were examined at this conference, 80 were obtained from syphilitics and the others from nonsyphilitics, chiefly from persons with neurologic diseases. For various reasons, such as cloudiness or contamination, only 67 spinal fluids were examined. The best results were obtained with the Harrison-Wyler Wassermann reaction, but the Müller and Kahn tests gave almost as good results.

After the conclusion of the conference in Copenhagen, Harrison, Wyler, and Kahn (*49*, *108*) went to London where they carried out simultaneous tests on 555 spinal fluids of which 508 were obtained from syphilitics. The Harrison-Wyler modification of the Wassermann reaction was done by Wyler and the Kahn reaction by Kahn. About half of the fluids were cloudy and were reported separately. Of the clear fluids obtained from syphilitics there was substantial agreement between the two tests in approximately 75 percent. In the cloudy specimens the agreement was 72 percent; in this series the preponderance of positive reactions was more pronounced in the case of the Wassermann test. There were no disagreements or nonspecific reactions in nonsyphilitic control fluids. In all groups of syphilitic spinal fluids, treated and untreated, clear and cloudy, the Kahn test gave 241 positive, 27 doubtful, and 240 negative reactions, while the Wassermann test gave 240 positive, 73 doubtful, and 195 negative reactions. Although Kahn states that the plus-minus reaction of the spinal fluid is of no value, Wyler is of the opinion that practical experience has shown that plus-minus reactions in spinal fluid are of considerable value, particularly when recurring in subsequent tests, not only for diagnostic purposes but also in following the effect of treatment. When the plus-minus results are included in the positive results (as they are interpreted in known cases of syphilis) the Kahn tests gave 268 positive results against 313 positive results by the Wassermann test. It is also to be remembered that the laboratory technic of the Kahn test is more complicated when applied to the examination of spinal fluid than to the examination of serums. Another point which comes to mind is the question in regard to the sensitivity of the Harrison-Wyler modification of the Wassermann test. Its sensitivity at the Copenhagen conference was only 41.8 percent. One does not know whether it was more sensitive as performed in London during the comparative studies with the Kahn test or not, and if more sensitive, how much more sensitive was it?

Müller (*96*) points out that it was decided at this conference that a Wassermann test on the spinal fluid should by no means be omitted. For this reason alone, he states, every laboratory should have the facilities for doing Wassermann reactions.

In 1930 a third serologic laboratory conference was held in Montevideo (*50*). Of the seven Wassermann modifications done, six were those of South American serologists, whereas the seventh was that of Harrison and Wyler of London. Five flocculation tests were represented which included the Meinicke clarification reaction, the Müller clotting reaction II, the Prunell serohemoflocculation reaction (Prunell of Montevideo), the Kahn standard, and the Kahn presumptive reactions. Here again Kahn's flocculation reaction was the only test represented from the United States. The Wassermann reaction as modified by a United States serologist was not represented. The Kahn standard test was the most sensitive of the tests which gave no false positive reactions. The Müller reaction II was 8 percent more sensitive than the standard Kahn test, but there were two false positive reactions. The Kahn presumptive test was 18 percent more sensitive than the standard Kahn test but gave three false positive reactions.

Approximately 200 specimens of spinal fluid were tested. The Kahn test and the Harrison-Wyler modification of the Wassermann gave no false positive reactions in 147 nonsyphilitic fluids. Out of 53 specimens of spinal fluid from cases of treated and untreated neurosyphilis, the Kahn test gave positive results in 33 and the Harrison-Wyler Wassermann in 28. The presumptive Kahn test gave 35 positive reactions in this group and 4 false positive reactions in the nonsyphilitic group. As a basis for comparison of the Kahn standard with the Harrison-Wyler Wassermann test it is to be pointed out that as tested on blood serums, the Kahn standard test had a sensitivity of 63.9 percent and the Harrison-Wyler test a sensitivity of 54.4 percent.

The committee again advised that both a Wassermann and a flocculation test be used simultaneously in the serum diagnosis of syphilis.

United States Evaluation Study No. 1

In 1934 the Surgeon General of the United States Public Health Service appointed the Committee on Evaluation of Serodiagnostic Tests in the United States consisting of two clinical pathologists (chosen by the American Society of Clinical Pathologists), two syphilologists, and two officers of the United States Public Health Service to develop a method for the evaluation of serodiagnostic tests for syphilis in the United States. The plan decided upon was to collect samples of blood obtained from patients in various stages of syphilis, from normal, nonsyphilitic persons, from patients with various diseases, and from pregnant, nonsyphilitic women. These samples were then to be redistributed to the laboratories of participating serologists. The serologists participating in this evaluation study were those who had described an original serologic test or a modification of a preexisting test. Those who had described more than one serologic test delegated the performance of the second test to another laboratory in a different city. Spinal

fluid samples were obtained from nonsyphilitic persons with nervous and mental diseases and from neurosyphilitic patients who were institutionalized. All tests were to be reported as positive, doubtful, and negative. The percentage of specificity of a given test was to be estimated from the presumably nonsyphilitic persons and the percentage of sensitivity from the known syphilitic patients. The doubtful reports were to be evaluated as a separate group on the basis of specificity and sensitivity.

For the sake of consistency and simplicity, only the five tests which are the subject matter of this paper will be discussed. For complete reports of the evaluation studies the original articles should be consulted (*17*, *39*).

In this evaluation study the Eagle complement fixation test was not included. A Hinton test suitable for the examination of spinal fluid had not yet been developed, and for this reason Hinton did not participate in the evaluation study of tests for spinal fluid.

The following are, in brief, the results obtained in regard to specificity and sensitivity with these five tests:

Specificity on serums.

Kolmer, Kahn, Kline diagnostic	No false positives.
Kline exclusion, Hinton	0.7 percent false positives.
Eagle	2.0 percent false positives.
Kahn presumptive	3.3 percent false positives.

Sensitivity on serums.

1. Untreated primary syphilis:

	Percent
Kahn presumptive	82.9
Hinton	81.0
Kline exclusion	80.5
Kahn standard	76.7
Kline diagnostic	74.4
Eagle flocculation	72.1
Kolmer	65.9

2. Untreated secondary syphilis:

All tests were 100 percent positive.

3. Late syphilis:

	Percent
Hinton	84.5
Kahn presumptive	84.3
Kline exclusion	83.0
Eagle flocculation	82.4
Kahn standard	76.9
Kolmer	72.1
Kline diagnostic	65.9

In regard to sensitivity, the following percentage of doubtful results were obtained with the various tests in the entire group of syphilitics: Kline 6.1 percent, Hinton 4.2, Kahn 4.1, Kolmer 3.2, Kahn presumptive 1.0, and Eagle 0.7 percent.

Specificity on spinal fluids (110 nonsyphilitic persons).

Eagle flocculation	No false positives; no false doubtful rcactions.
Kolmer	No false positives; no false doubtful reactions.
Kahn presumptive	No false positives; no false doubtful reactions.
Kahn standard	No false positives; 2.7 percent false doubtfuls.
Kline	1.0 percent false positives; no doubtful reactions.
Kline exclusion	No false positives; no false doubtfuls.

Sensitivity on Spinal Fluids (110 neurosyphilitic patients).

Kahn	92.5 percent (2 doubtfuls).
Kline	89.4 percent (2 doubtfuls).
Kahn presumptive	88.0 percent (7 doubtfuls).
Kline exclusion	79.1 percent (11 doubtfuls).
Eagle	78.0 percent (4 doubtfuls).
Kolmer	77.8 percent (3 doubtfuls).

When, instead of only nonsyphilitic normal persons being included in the group used to test for specificity of the various tests, pregnancy and special disease groups such as tuberculosis, cancer, fever, and jaundice were added to the nonsyphilitic group, the results obtained on the serums were somewhat different, as follows:

Specificity.

Kahn presumptive	3.0 percent false positives; 1.7 percent doubtful.
Hinton	1.7 percent false positives; 4.8 percent doubtful.
Eagle	1.1 percent false positives; 1.0 percent doubtful.
Kolmer	0.7 percent false positives; 0.2 percent doubtful.
Kahn	0.2 percent false positives; 0.9 percent doubtful.
Kline	0.2 percent false positives; 0.0 percent doubtful.

Percentages of positive serologic tests for syphilis in nonsyphilitics with various other diseases, in the febrile state, and in pregnancy, were as follows:

Leprosy.—The percentages of positive results obtained in 50 cases of leprosy were: Eagle 72, Kline 66, Kolmer 64, Kahn 60, and Hinton 40.

Tuberculosis.—The percentages of positive results obtained in 53 cases of tuberculosis were: Hinton, 5.7, Kolmer 2.0, Kahn, Kline, and Eagle each 1.9.

Malignancies.—The percentages of positive results obtained in 62 cases of malignancies were: Hinton 3.3, Eagle 1.7, Kolmer 1.6. No positive results in this group were obtained with the Kahn and Kline tests.

Natural or induced fever.—The percentages of positive results obtained in 46 cases of natural or induced fever were: Hinton 2.3 and Kolmer 2.2 The Kline, Kahn, and Eagle tests gave no positives in this group.

Malaria.—The percentages of positive results obtained in 36 cases of malaria were: Kolmer 19.4, Kline 14.3, Eagle 12.1, Kahn 11.4, and Hinton 11.1.

Jaundice.—No positives were obtained in 51 cases.

Pregnancy.—In 54 cases of pregnancy only the Hinton test gave positive results, namely in 1.9 percent of cases.

Women during the menstrual as well as the intermenstrual periods.—No positives were obtained with any of the tests.

Since all of the serologists reported a very high percentage of positive serologic reactions among the presumably nonsyphilitic lepers, these patients were reexamined for the possible presence of syphilis (*38*). The examination included roentgenologic examination of the long bones and of the aorta but did not include spinal puncture. All patients in this group were believed to be free of frambesia and all with the probable exception of 6, free of syphilis. It was observed that the patients with advanced clinical symptoms or those with many lepra bacilli were much more apt to show positive reactions. This group of 50 patients was reexamined serologically. In this second study 15 patients (30 percent) had positive or doubtful reactions to all tests; 4 (8 percent) had uniformly negative reactions; in 31 (62 percent) there was more or less discrepancy in the results.

According to the reports in the literature most observers have found that presumably nonsyphilitic lepers frequently show positive serologic reactions for syphilis. Kolmer, who consistently claimed negative results in nonsyphilitic lepers with both the Kahn and the complement fixation tests, nevertheless reported 64 percent of positive results in this group. The patients used in this study were from the National Leprosarium at Carville, La., just as were those who formed the basis for Kolmer's previous studies. It is pointed out that various reports that antisyphilitic medication promptly causes the reactions to become negative are not to be taken as certain indication that the lepers are syphilitic.

Evaluation in regard to specificity of the tests applied to the examination of spinal fluid samples (*39*) shows that if doubtful reactions are included in the rating, only the Eagle, the Kahn presumptive, the Kline diagnostic (1 percent false positive reactions), the Kline exclusion, and the Kolmer tests showed more than 99 percent of specificity.

The percentage of sensitivity of most of the tests carried out on the spinal fluid was less than one would expect in general paresis (101 of the group of 110 were cases of general paresis). This was attributed to the fact that most of the patients had received considerable treatment with tryparsamide or had had malarial therapy. The percentage of sensitivity was much higher when only a group of 39 patients who had received little or no treatment was considered.

Comparison of the most efficient flocculation tests with the most efficient complement fixation tests in this study showed that there was little difference between them.

The conclusions reached by the committee after this evaluation study were as follows:

1. This study indicates relatively equal value to the clinician of efficient complement fixation tests and efficient flocculation tests as applied to either

blood or spinal fluid specimens. This study further reveals that while most flocculation tests are approximately equal in value to complement fixation tests when applied to spinal fluid specimens, it is apparent that certain of the flocculation methods are relatively inadequate.

2. The studies of the committee, based solely on the information derived from the evaluation of these reports, show that if two tests are to be performed, it is immaterial whether two complement fixation tests, two flocculation tests, or a combination of one flocculation test and one complement fixation test are selected.

3. As regards specificity of spinal fluid examination, it is probable that the test should rate at least 99 percent. As regards sensitivity the test should rate at least 90 percent.

4. If no penalty is imposed for doubtful reports in the spinal fluid, the following tests are satisfactory as regards specificity: Eagle, Kahn presumptive, Kahn standard, Kline exclusion, Kline diagnostic, and Kolmer. If these are penalized for doubtful reports, the Kahn standard tests fails to qualify by a narrow margin.

As regards sensitivity, it would seem that the figures should be based on patients who have received no malaria, or less than 12 injections of tryparsamide, or less than 15 injections of arsphenamine. The tests qualifying for sensitivity are the following: Eagle, Kahn standard, Kahn presumptive, Kline diagnostic, and Kline exclusion. If sensitivity is rated on the well-treated, poorly treated, and untreated cases of neurosyphilis, only the Kahn standard test qualifies.

5. The results of this study indicate that it is satisfactory to report results merely as positive, doubtful, or negative.

The evaluation of doubtful results.—Although the committee planned to evaluate doubtful reports in this study as a separate group on the basis of specificity and sensitivity, "there was no general agreement in the proposals offered by the participating serologists for the evaluation of this group of reports" and "doubtful" results were not even mentioned in the widely publicized preliminary reports. Also, in the preliminary report, tests for specificity were applied only to the group of 152 normal individuals and did not include the 317 presumably nonsyphilitic patients with various diseases. Such omissions, for the sake of simplicity and clarity, are not satisfactory from the standpoint of the clinician, as Moore (*91*) has pointed out. In the final report correction was made in this respect and doubtful results as well as tests of specificity on the entire group of 469 patients were published, as has already been shown in this paper.

In spite of the fact that doubtful results are difficult to evalue, it is obvious, as Moore has pointed out, that although a doubtful result in a known syphilitic patient is not as convincing as a positive result, it should nevertheless be scored as a partial success for the competing serologist. Conversely,

while a false doubtful result in a nonsyphilitic person is not as disturbing to the clinician as a false positive result, it is nevertheless disturbing enough and as such is to be rated as a partial failure for the serologic test in question. Doubtful serologic reactions may be due to syphilis, as a stage in the appearance of reagin early in the disease, or in its disappearance later, especially under the influence of treatment. In nonsyphilitic persons, doubtful results may be due to technical error, to faulty interpretation, to attempts to increase the sensitivity of a given test beyond its particular limits of safety, or to the same biologic phenomena which, rarely, cause a false positive result.

In discussing this evaluation study Moore makes some pertinent comments. He states that the clinician desires that the laboratory shall employ a test which is positive in the highest possible percentage of patients infected with syphilis (maximum sensitivity) but which is uniformly negative in nonsyphilitic individuals (maximum specificity). No test as yet devised has absolute specificity or absolute sensitivity. In general, sensitivity is increased at the expense of specificity or vice versa. To the clinician interested primarily in diagnosis, specificity is a more important factor than sensitivity. It is particularly desirable to employ as a routine diagnostic test one which provides the smallest possible number of nonspecific reactions (whether positive or doubtful) in nonsyphilitic persons. A diagnosis of syphilis made in an uninfected individual is a disaster of the first magnitude. If maximum specificity demands some sacrifice of sensitivity, the clinician is quite willing to accept the sacrifice. The complement fixation and flocculation tests depend on identical physiochemical phenomena and differ from each other only in certain technical details. The former is harder to do, requiring more ingredients, but easier to read; the latter is simpler, but harder to read. Since no test is as yet so sensitive as to detect all instances of syphilitic infection, a negative result does not exclude the presence of syphilis. The proper person to interpret serologic results is not the serologist but the clinician who can fit the laboratory data with history and physical findings.

In ranking the tests in the order of their comparative specificity and sensitivity (in regard to studies on the blood only), using as a satisfactory standard of specificity that chosen by the serologists at previous conferences, namely, less than 1 percent of false positive tests in nonsyphilitic persons, Moore found that seven tests qualified as satisfactory. When, however, false doubtful results were added to the false positives, only four were satisfactory, namely, the Kline diagnostic, the Kolmer, the Kahn diagnostic, and the Brem complement fixation tests.

United States Evaluation Study No. 2

The same agencies which planned and carried out the first evaluation study were also reponsible for the second, somewhat different evaluation

study (*101*, *40*). Since the criterion by which any laboratory procedure may be expected to stand or fall is its efficiency in hands other than those of its originator, it was decided in this second project to send samples of each specimen to several laboratories, including the laboratory of the originator of the particular test under consideration. It was decided that the results of such an evaluation would be a much better indicator of the efficiency of the various tests under everyday working conditions in the serologic laboratory.

Of 39 directors of State, municipal, or private laboratories who expressed a desire to participate in this study, it was possible, because of limitation of funds, to select only 30. Selection was made on the basis of priority of requests or the strategic position of the laboratory in furthering the program for the control of syphilis in this country. Included were serologists of 11 State, 5 municipal, and 14 private laboratories. The Eagle flocculation test was done by 1 laboratory, the Hinton by 1, the Johns flocculation by 1, the Kahn presumptive by 2, the Kahn standard by 12, the Kline diagnostic by 7, the Kline exclusion by 2, and the Kolmer test by 14 laboratories. The originator of each of these serologic methods performed an examination on a comparable sample of blood in order that the study might be properly controlled. The remaining 11 performances comprised a heterogeneous group of serologic tests which had not been given consideration in the first study. With the exception of the Eagle complement fixation (1 laboratory) and the micro-Hinton tests (1 laboratory) no control tests were made for this heterogeneous group.

Approximately 200 specimens were from known syphilitic donors and approximately 100 were from normal, presumably nonsyphilitic donors. Among the syphilitic donors there were about 10 with untreated secondary syphilis and about 190 who had received varying amounts of treatment.

Sensitivity of control performances:

Hinton	88. 8 percent (5 doubtful reports).
Kline diagnostic	88. 8 percent (10 doubtful reports).
Kline exclusion	84. 8 percent (14 doubtful reports).
Eagle complement fixation	83. 8 percent (8 doubtful reports).
Kahn presumptive	79. 6 percent (5 doubtful reports).
Eagle flocculation	77. 8 percent (no doubtful reports).
Kahn standard	75. 7 percent (3 doubtful reports).
Kolmer	59. 0 percent (1 doubtful report).

Specificity of control performances:

Kolmer	100. 0 percent (no doubtful reports).
Eagle complement fixation	100. 0 percent (no doubtful reports).
Eagle flocculation	100. 0 percent (no doubtful reports).
Hinton	100. 0 percent (no doubtful reports).
Kahn standard	100. 0 percent (1 false doubtful report).
Kline exclusion	100. 0 percent (4 false doubtful reports).
Kline diagnostic	99. 03 percent (1 false positive, 1 false doubtful).
Kahn presumptive	98. 98 percent (1 false positive, no false doubtfuls).

In some of the State and local laboratories the serologic testing did not compare favorably with the results achieved in the laboratories of the originators of the methods. In others, however, the results obtained were at least comparable to those obtained in the control laboratories. The committee advised that some of the tests should either be modified to increase their sensitivity or specificity or both, or be abandoned. It was pointed out that an efficient serodiagnostic test for syphilis should possess 100 percent specificity; any test which yields even 1 percent of false positive reactions should be so modified as to increase its specificity, even with some slight sacrifice of sensitivity. A diagnosis of syphilis, unsupported by history or clinical evidence, should never be made on the basis of a single positive blood reaction. In such case the test should be repeated in the same laboratory, or in another laboratory, utilizing two or more different tests.

The committee further decided that if two tests are to be performed, it is immaterial whether two efficient complement fixation tests, two efficient flocculation tests, or a combination of one efficient flocculation test and one efficient complement fixation test is selected. It was found satisfactory to report the results of qualitative tests as merely positive, doubtful, or negative. Again, no attempt was made to evaluate doubtful reports.

The directors of laboratories performing serodiagnostic tests for syphilis were advised to avail themselves of the opportunity of comparing their results with those of well-qualified serologists in other laboratories performing the same test on comparable samples from known syphilitics and presumably nonsyphilitic persons. It was advised that this system of comparative examination of tests be extended annually to all State laboratories. In turn the State laboratories should offer similar opportunity to local laboratories.

United States Evaluation Study No. 3

The results of the second evaluation study showed that although many of the State and local laboratories were highly efficient in the performance of serodiagnostic tests for syphilis, there were others whose standards were too low for them to be able to serve as control laboratories for the local laboratories within their boundaries. The committee therefore recommended that the United States Public Health Service make an annual comparison of serodiagnostic tests for syphilis done by all State laboratories. The Surgeon General of the United States Public Health Service invited the health officers of the 48 States and the District of Columbia to participate in the third evaluation study (*102*). The invitation was accepted by the health officers of 39 States. Each health officer was asked to designate the test or tests whose performance he desired to have evaluated. The tests specified determined the choice of the methods to be

employed as control tests. Therefore, the laboratories of Hinton, Kahn, Kline, and Kolmer, whose tests were selected, served as control laboratories.

The serums of 100 presumably nonsyphilitic donors (chiefly medical students) were used for determinations of specificity and those of 200 syphilitic patients were used for determinations of sensitivity of the tests. Five percent of the syphilitic donors had early secondary syphilis. The remainder was composed of persons who had had syphilis for a longer period of time and who had received varying amounts of treatment. Most of the laboratories performed two, some three tests, and 8 only one test.

Sensitivity of control performances.

Kline exclusion	96.5 percent (5 doubtful reports).
Hinton	92.9 percent (4 doubtful reports).
Kahn presumptive	91.8 percent (3 doubtful reports).
Kolmer	88.2 percent (no doubtful reports).
Kahn standard	84.5 percent (4 doubtful reports).
Kline diagnostic	83.9 percent (19 doubtful reports).

Specificity of control performances.—All of the tests received a 100-percent specificity rating. However, whereas no false doubtful reports were obtained with the Kolmer, the Kahn standard and the Kline diagnostic tests, the Hinton test gave one, the Kahn presumptive one, and the Kline exclusion three false doubtful reports.

The results of this evaluation study revealed that some of the State laboratories were not qualified to perform efficient serodiagnostic tests nor to inaugurate any system of State licensure or approval of local laboratories within their respective States. On the other hand, in many of the State laboratories, the performance of serodiagnostic tests for syphilis was highly efficient and compared favorably with the control tests as carried out by the originators of the methods. In some of the laboratories performing more than one test for purposes of evaluation, one of the tests was performed in an efficient manner while the other gave poor results. Several laboratories entered tests which they did not use as a routine in order to determine their ability to perform such tests efficiently. Many of the tests that were designated as Hinton, Kahn, Kline, or Kolmer tests by the performers were so modified that it would be an injustice to the originators of the methods to refer to them as such.

This study further showed that the routine employment of a single serodiagnostic test, although performed by competent workers, is occasionally unreliable. If a single test is used as a routine, the laboratory should be prepared and willing to carry out a second test with a different method upon request.

The committee made the following recommendations to State health officers:

1. That provision be made for adequate training of State and local laboratory technicians in the laboratories of the originators of the methods

employed in the respective laboratories and that in the future only thor oughly competent technical personnel be employed. Funds being mad available to the States under the provisions of the Social Security Act an allotted for the training of personnel should be utilized for the tuition an stipend of the State and local laboratory technicians.

2. That a system of periodic inspection of State laboratories by thor oughly trained serologists of the United States Public Health Service b inaugurated and made available upon the request of State health officers and that advantage be taken of the system of comparative examination o serodiagnostic tests for syphilis to be extended annually by the Unite States Public Health Service.

3. That the facilities available for special study of serologic methods i the Venereal Disease Research Laboratory of the United States Publi Health Service at Stapleton, Staten Island, N. Y., be further utilized fo the training of personnel from State laboratories.

4. That the need is again emphasized for the development by Stat laboratories of a system of periodic comparative examination of the per formance of serodiagnostic tests by municipal, hospital, and private labor atories located within the respective States.

5. That full advantage be taken of existing local laboratory facilities an that provisions be made to approve and to subsidize qualified local labora tories for the performance of diagnostic services in the control of syphilis.

United States Evaluation Studies No. 4 and No. 5

In an evaluation study carried out in 1938 (*42*), 46 laboratories, repre senting 44 States and the District of Columbia, took part. A total of 9 test procedures, which included 33 complement fixation, 49 diagnosti flocculation, 10 supersensitive (exclusion or presumptive) flocculation pro cedures as well as 4 flocculation technics which could not be accurate classified since they followed no known standard technic, were carried ou

In 1939 (*42*), 38 State and 3 Public Health Service laboratories partici pated. A total of 97 test procedures were carried out which included 3 complement fixation and 66 flocculation procedures. The number c laboratories which adhered to standard technics had greatly increased sinc 1938. Only 12 of the 43 which failed to follow the authors' rules in 193 still did not use a standard technic in 1939.

The committee points out that the level of sensitivity of the control per formances in 1939, as compared to that in 1938, was somewhat higher. Evi dently the 1939 group of donors contained a greater number of individual with more reagin in their blood. The relative position of the control per formances in regard to sensitivity was somewhat altered in 1939. The Hin ton test, which for a number of years had been the most sensitive, took position below the Kline exclusion and the Kahn presumptive tests in 193

Sensitivity of control performance

	1938	1939
	Percent	*Percent*
Kline exclusion	83.3 (11 doubtful)	91.0 (2 doubtful)
Kahn presumptive	79.1 (2 doubtful)	87.6 (1 doubtful)
Hinton	83.9 (3 doubtful)	85.5 (6 doubtful)
Kolmer	78.2 (1 doubtful)	83.4 (no doubtful)
Eagle microflocculation	77.5 (5 doubtful)	82.4 (7 doubtful)
Eagle macroflocculation	.....	80.2 (5 doubtful)
Kline diagnostic	73.4 (13 doubtful)	78.7 (20 doubtful)
Kahn standard	70.5 (9 doubtful)	77.4 (18 doubtful)
Eagle complement fixation	72.2 (10 doubtful)	73.9 (8 doubtful)

Specificity of control performances.—In the 1938 study none of the control serologists reported a single instance of a false positive or a false doubtful reaction. In the 1939 evaluation study all of the control serologists, except two, had a perfect record in this respect. The Kline exclusion test was penalized by the fact that one nonsyphilitic donor's blood gave some degree of positivity to all Kline tests. The Kline diagnostic procedure was doubtful. A repeat specimen gave almost identical results. Hinton's laboratory also gave one false positive report. Since all other control tests and the Hinton tests done in other laboratories were negative, it seems probable that this represents a laboratory error.

The Committee set the criteria for satisfactory results as follows:

For sensitivity (the percentage of true positive reactions from known syphilitic donors) the result must not be more than 10 points below that of the control laboratory. For example, if the control laboratory had a sensitivity of 91.2 percent, the lowest rating that could be considered satisfactory would be 81.2 percent.

For specificity (the percentage of negative and doubtful reactions from presumably nonsyphilitic donors), the result must not be lower than 99 percent.

Doubtful results.—Because of the fact that no agreement existed among the various serologists as to what penalties or awards should be given for doubtful reactions, the committee gave a negative rating to all such reports. It was fully realized, however, that false doubtful reports on normal serums should count definitely against a laboratory and that in known cases of syphilis a doubtful reaction may be of great value.

Work done in State laboratories.—The results of these evaluation studies showed that, whereas in 1938, 30 State laboratories were unsatisfactory in their performance of at least 1 test, only 22 were unsatisfactory in 1939, and 18 of these 22 laboratories have expressed dissatisfaction with their results and have taken steps to improve them.

In 1938, 10 State laboratories approximated the results of the control.

laboratories, and 5 reported results which were considered satisfactory. In 1939 the 10 laboratories which approximated the results of the control laboratories in 1938 did not participate in the study. During the 1939 study, 3 State laboratories reported results which were comparable to those of the control laboratories, with the exception of the unsatisfactory performance of an ultrasensitive test by one of them. Thirteen other laboratories reported results which were considered satisfactory. If the 10 State laboratories which did not participate in 1939 because of superior performance in 1938 are included, a total of 26 laboratories can be considered to be performing satisfactory tests.

The 1940 serodiagnostic evaluation study will include the performances of each State and the District of Columbia and will be carried out in the same way as the studies of the immediately preceding years.

Special Studies

Effect of tuberculosis on serodiagnostic tests for syphilis.—Quite recently the Committee on Evaluation of Serodiagnostic Tests in the United States sponsored another study to determine the effect of tuberculosis on the serologic reactions for syphilis (*103*). Five originators of serologic methods, namely, Eagle, Hinton, Kahn, Kline, and Kolmer, took part in this study. Nine tuberculosis sanatoria, recommended by the National Tuberculosis Association, contributed serums from white patients with moderately or far advanced pulmonary tuberculosis. Insofar as possible, coincident syphilis infection was excluded. Each sanatorium contributed serums from approximately 50 tuberculous donors and from 10 to 15 syphilitic donors. Two complement fixation tests (Kolmer and Eagle), 4 diagnostic flocculation tests (Eagle macroflocculation, Hinton, Kahn standard, and Kline diagnostic) and 2 supersensitive flocculation tests (Kahn presumptive and Kline exclusion) were carried out with the blood of each donor, each test being performed in the laboratory of its originator. In cases which revealed any appreciable degree of serologic discrepancy among the laboratory reports a second blood specimen was distributed, and a detailed clinical resurvey of the donor as to the possibility of infection with both syphilis and tuberculosis was carried out.

Of the 458 supposedly nonsyphilitic tuberculous donors the serums of 8 were found to be positive to many laboratory tests. In 4 of these a careful review of the patients' histories revealed evidence which supported the probable presence of syphilitic infection. Three of the remaining ones were not available for reexamination, while in one the recheck failed to reveal history or clinical evidence indicative of syphilis.

In the remaining 450 serums the Kolmer and Kahn standard tests gave negative results, whereas 1 positive was obtained with the Eagle macroflocculation and 1 positive and 10 doubtfuls with the Eagle complement

fixation test. The Kline diagnostic test recorded 4 doubtful reactions and the Hinton 4 positive and 8 doubtful reactions. Of the so-called supersensitive methods the Kahn presumptive recorded 1 positive and 1 doubtful and the Kline exclusion 5 positive and 11 doubtful reactions.

Of the original findings with the Hinton test 5 of the doubtful and 3 of the positive reactions were reversed to negative in recheck specimens. With the Kline exclusion test 4 doubtful and 2 positive reactions reversed to negative on the second examination. This test, however, recorded 2 positives on reexamination which were doubtful with the original specimens and 2 doubtfuls which were negative in the original serums.

The conclusions of the committee on the basis of this evaluation study were: "Inasmuch as with the present serologic tests for syphilis both typical and atypical false doubtful and false positive results are found in serums from tuberculous donors, it is evident that tuberculous toxemia may contribute a confusing factor to syphilis serology. It should not, however, present a major problem in the clinical interpretation of results obtained with carefully conducted serodiagnostic procedures."

Effect of malaria on serodiagnostic tests for syphilis.—A study of patients with malaria was included in the evaluation of serodiagnostic tests which was reported in 1935 (*17*). A total of 457 tests of specimens from 36 malarial donors were studied, and there were 66 (14.4 percent) of positive reactions and 28 (6.1 percent) of doubtful reactions. The results obtained by the 13 serologists who participated in this study were in complete agreement in only 14 of the 36 patients. The results of repeat tests rarely agreed with the original results, varying as much from each other as complete positive and complete negative.

A second study (*41*) was reported in 1938 which included a total of 266 patients. These were all white persons from South Carolina and Georgia whose history and physical findings gave no indication of syphilitic infection. The tests performed were the Hinton, Kline (diagnostic and exclusion), and Kolmer tests.

The percentage of positive reports obtained in this study was not as high as that of the first study but was higher than would be expected among white persons who are presumably nonsyphilitic. The results were as follows:

Hinton	4.4 percent of positive reports; 12 doubtful reports.
Kolmer	4.9 percent of positive reports; no doubtful reports.
Kline diagnostic	6.2 percent of positive reports; 17 doubtful reports.
Kline exclusion	16.2 percent of positive reports; 22 doubtful reports.

For 191 patients (71.8 percent), all examiners recorded negative findings, and for 6 patients (2.3 percent) all reported positive findings. For 69 patients (25.9 percent) the results disagreed. There were altogether 82 positive and 51 doubtful reports. On repetition of the tests it was found

that the number of repeatedly positive reports dropped to 56. An interesting finding was that among 68 specimens of serum obtained from 18 white girls less than 10 years of age there were 13.2 percent which gave a positive reaction which was the highest percentage in any age group except that from 60–69 years. Women showed a higher percentage of positive results than men. These findings do not follow the usual trend of the prevalence of syphilis.

Analysis of Evaluation Studies

The problem of analyzing the results obtained at the serologic laboratory conferences in Copenhagen and Montevideo as well as of the evaluation studies carried out in the United States in an attempt to establish in a definite manner the relative value of the tests is a very difficult one. It is apparent, first of all, that the same test gives variable results. It may show up very well at one evaluation study and give much poorer results at another. For example, the Kolmer test showed 72.1 percent of sensitivity (late syphilis) in 1934, 59.0 percent in the second, 88.2 in the third, 78.2 in the fourth, and 83.4 in the fifth study. The standard Kahn test in these same studies gave the following percentages of sensitivity: 76.9, 75.7, 84.5, 70.5, and 77.4 respectively. Also, in the final published report of a study of this nature all of the factors which may have influenced the performance of a test are not apparent. For example, at the second Copenhagen conference the complement fixation tests made an extremely poor showing. The reason for this was not definitely known but it was apparently due to one or several factors such as external conditions, the complement used, the time factor. In spite of this poor showing, the serologists participating in the conference were aware, on the basis of their own experience, of the value of the complement fixation test, especially in the study of spinal fluids, and far from wanting to discard it, they definitely advised that both a complement fixation and a flocculation test should be used in the examination of every serum. Another factor is the unsatisfactory evaluation of doubtful results. One might be able to disregard doubtful results obtained in persons who have or have had syphilis. But in a presumably nonsyphilitic person a doubtful result is another matter, and a test procedure which gives doubtful results in nonsyphilitics is less valuable than a test which does not give such results. This criticism applies in particular to tests which give false doubtful results on spinal fluid, because repeating the spinal puncture is not an altogether simple procedure or one that is welcomed by the patient.

Wadsworth (*127*) points out that the accuracy of any evaluation is limited by the accuracy of the data on which it is based, and any abridgments of the fundamental information, such as the use of broad classifications, may sacrifice a part of this accuracy. This appears to be considerable, he says,

when the results of serologic tests are reported "positive," "doubtful," or "negative" as prescribed by the U. S. Public Health Service in its study of comparative tests, especially since no generally accepted basis exists for the classification. From the standpoint of aid to the clinician in diagnosis, the zone of the doubtful reaction may be conservatively broad or so narrow as to have no significance and to be definitely misleading. The doubtful zone is possibly the most important in any analysis of the practical value of serologic tests. Yet it has been neglected in the evaluation of these Federal series. Under these conditions, ratings based upon 100 percent specificity and percentage of "positive" reports are not only open to serious criticism but reflect on the relative efficiency of the "control tests," which should be considered in relation to present-day standards of serology and in the light of what is possible. Not all serums from patients with a syphilitic infection react, and reactions may occur when no evidence of syphilis can be found. Finally in rating percentages of specificity or sensitivity, apparently no account has been taken of the positive reports by the "control" laboratories on specimens of very slight activity or of negative reports on the serums of well-marked activity from cases of syphilis that had little or no treatment. If such a system of rating reflects on the "control tests," it may also reflect on or obscure the record obtained by some of the other laboratories.

Schoch (*42*), in the discussion at the close of the paper by the serologic evaluation committee expresses the hope that doubtful results will hereafter be properly evaluated. He points out that greater penalty should be put on tests that give false doubtful reports on presumably nonsyphilitic serums than credit received for true doubtful reports on serums which contain syphilitic reagin. Hazen at the close of the same discussion states that the committee has planned to deduct a half point for each false doubtful reaction and grant a credit of a half point for each doubtful report submitted on a syphilitic person.

CHOICE OF A SEROLOGIC TEST

Choice of test for serum.—A survey of the results obtained with the tests under consideration in all 5 of the evaluation studies in which they were used will now be made in order to ascertain, as far as possible, the relative value of the different tests on the basis of these findings. Only in the first evaluation study were the syphilitic patients classified as primary, secondary, and late syphilis. The Kahn presumptive, the Hinton, and the Kline exclusion tests were the most sensitive tests in primary syphilis, giving 82.9, 81.0, and 80.5 percent of positive reactions, respectively; the Kahn standard, the Kline diagnostic, the Eagle flocculation, and the Kolmer gave 76.7, 74.4, 72.1, and 65.9 percent of positive reactions, respectively, in primary syphilis. All of the tests were 100 percent positive in secondary syphilis. In late syphilis the Hinton, Kahn presumptive, Kline exclusion, Eagle

flocculation, Kahn standard, Kolmer, and Kline diagnostic tests gave the following percentages of positive reactions, respectively: 84.5, 84.3, 83.0, 82.4, 76.9, 72.1, and 71.5. However, a sensitive test is valuable only if it is specific at the same time; in fact, specificity is much more important than extreme sensitivity if a choice between the two characteristics has to be made. In the first evaluation study the Hinton gave 0.7 percent of false positive reactions, the Kahn presumptive 3.3 percent, the Kline exclusion 0.7 percent, the Eagle flocculation 2.0 percent of false positive reactions, the other tests having 100 percent specificity. In other words, the three most sensitive tests were also the most unreliable tests in this first study.

The results of the other four evaluation studies in regard to sensitivity were in brief the following:

	Hinton	Kline exclusion	Kline diagnostic	Kahn presumptive	Eagle flocculation	Kahn standard	Kolmer	Eagle complement fixation
	Percent	*Percent*	*Percent*	*Percent*	*Percent*	*Percent*	*Percent*	*Percent*
II	88.8	84.8	88.8	79.6	77.8	75.7	59.0	83.8
III	92.9	96.5	83.9	91.8	[1]	84.5	88.2	[1]
IV	83.9	83.3	73.4	79.9	77.5	70.5	78.2	72.2
V	85.5	91.0	78.7	87.6	82.4	77.4	83.4	73.9

[1] Not done.

The tests which gave false doubtful reactions in two or more of the four evaluation studies were the Hinton, Kline exclusion, Kahn presumptive, and Kline diagnostic tests. With the exception of the Kline diagnostic test, these, together with the Eagle flocculation test were also the least specific tests of the first evaluation study. The Eagle flocculation reaction was not included in the third study, and the Eagle complement fixation reaction was done only in the second, fourth, and fifth studies in which it was 100 percent specific. The most outstanding test in regard to specificity is the Kolmer test. In all five evaluation studies it was 100 percent specific and gave even among the syphilitic serums only 1 doubtful reaction. In the first two studies its sensitivity was rather low in comparison, being 72.1 (late syphilis) and 59.0 percent respectively. However, in the last three studies its sensitivity compares very favorably with that obtained with other tests which were less specific. Specificity should always be the most important requirement of a serologic test for syphilis. If a few diagnoses are missed in primary syphilis (where the dark field is the important diagnostic procedure) and in late and treated syphilis, it is not by any means so serious an error as placing a diagnosis of syphilis on a person who does not have the infection.

The Kahn presumptive and Kline exclusion tests are not specific enough to be used as diagnostic tests. This is definitely shown in these studies. Since the Eagle complement fixation reaction was used in only three evaluation studies, an adequate comparison between it and the Kolmer test cannot be made.

Choice of test for cerebrospinal fluid.—The basis on which the choice of a test for spinal fluid must be made consists of first, evaluation studies and second, the experience of the originators and their coworkers in their own laboratories, using both flocculation and complement fixation tests. The results of other studies which have been reported on such comparisons cannot be relied upon because of the inferior or questionable value of the complement fixation test used for comparison.

At the Copenhagen, London (spinal fluids only), and Montevideo conferences the Harrison-Wyler modification of the complement fixation reaction had a sensitivity of only 41.8 and 54.4 percent. At Copenhagen and London this test made a slightly better showing than the Kahn test and at Montevideo the reverse was true. On the basis of this comparison, the Kahn test must be considered to be inferior in sensitivity to the Kolmer complement fixation reaction which has much greater sensitivity than that shown by the Harrison-Wyler modification at these conferences.

The only evaluation study in the United States in which spinal fluid tests were done was the first one in 1934 (*39*). All of the tests except the Kolmer were flocculation tests. The results are quite surprising in the light of what experience has taught about the tests. For example, the Kahn presumptive test and the Kline exclusion test, the so-called "screen tests" which are considered to be very sensitive and not as specific as the other tests, gave 100 percent specificity and had a comparatively low sensitivity. The Kahn standard test was the most sensitive test (92.5 percent) but gave 2.7 percent of doubtful reactions on nonsyphilitic spinal fluids. The disadvantage of false positive tests on spinal fluids has already been pointed out. The Kline diagnostic test which was next to the Kahn in sensitivity (89.4 percent) gave 1.0 percent of false positive reactions. Another disadvantage of the Kline test is that it cannot be applied to spinal fluids which give a negative reaction for sugar. In other words, the spinal fluids have to be fresh, and many laboratories are not able to obtain fluids which are uniformly fresh (positive for sugar).

The second point, the results obtained by the originators of tests in their own laboratories, needs now to be considered.

Keim and Kahn (*55*) in 1925 studied 1,000 spinal fluids obtained from 382 patients. The results obtained show that the Kahn test was less specific and also less sensitive than the "18 hour ice box Wassermann reaction" as shown by the results obtained in the group of patients with general paresis and those having no involvement of the central nervous

system. Since that time, however, Kahn, who recognized this lack of sensitivity of the Kahn test for spinal fluids, has modified the technic and now concentrates the spinal fluid globulin before testing the spinal fluid (see technic of the Kahn test (*124*)). With the exception of the evaluation study of 1934, however, no comparisons of the Kahn technic and the complement fixation reactions have been published.

The Kline test for spinal fluid, which was not published until 1931, has apparently not been widely used. Spiegel, Eller and Rein (*116*) found it to be more sensitive than the Kahn and "Wassermann" reactions. Heathman and Higgenbotham (*43*) point out the disadvantage of the Kline test not being applicable to spinal fluids having a negative reaction for sugar. They compared it with the Kahn and Kolmer tests and found the Kolmer to be superior to either flocculation test.

In regard to the Eagle flocculation test, it is of interest to consider Eagle's (*25*) discussion of flocculation tests as applied to the examination of spinal fluids. He examined a total of 614 spinal fluids obtained from previously diagnosed and treated syphilitics by means of the Kahn, the Eagle flocculation, and the Eagle complement fixation tests. He found that only 67 of the 97 Wassermann positive or doubtful spinal fluids were detected by the Eagle flocculation test and that the Kahn test was even less sensitive. Moreover, the outcome of the flocculation test depended on the amount of reagin present in the fluid and could usually be predicted from the "strength" of the positive Wassermann reaction. Whenever the complement fixation reaction was positive with as little as 0.05 cc. of fluid, the flocculation test (with 1 cc. of fluid) was usually also positive. As the amount of the reagin in the fluid decreased, however, negative flocculation tests began to appear. Roughly, the complement fixation reaction proved to be 2½ to 3 times as sensitive as the flocculation test, requiring only ⅔ to ⅓ as much reagin in order to yield a positive reaction. He goes on to say that the above has been the experience of most serologists who have attempted to apply flocculation tests to spinal fluid. Recognizing the difficulty, Kahn developed a new procedure for the examination of spinal fluids, involving the precipitation of the spinal fluid globulin (containing the active reagin) by approximately half saturation with ammonium sulfate and redissolving the precipitate in a minimum volume of physiologic salt solution and using this concentrated globulin solution in a flocculation test. Eagle points out, however, that in his laboratory this procedure has proved entirely unsatisfactory for the following reasons: Even with reasonable care in the removal of the supernatant ammonium sulfate solution after the centrifuging of the globulin precipitate, so much ammonium sulfate remains in the precipitate that when the antigen suspension is added to its solution, there is a nonspecific aggregation due to excess electrolyte which simulates the aggregation due to reagin. Another and

more serious objection is the finding that the procedure usually yields no globulin precipitate in the very spinal fluids in which the ordinary flocculation test is negative and the Wassermann test positive, that is, the very fluids in which the procedure should find its application. Of the 24 fluids in Eagle's series falling into this category, all but 5 gave a negative or weakly positive Pandy test, and a flat or nearly flat mastic curve; in other words, at least 75 percent of these positive fluids contained so little globulin that no significant precipitate would form upon half saturation with ammonium sulfate. Full saturation of such fluids does yield a precipitate consisting almost entirely of the normal spinal fluid protein plus any reagin or globulin which may have been present; but such a saturated solution has so high a specific gravity that the protein will not sediment clearly upon centrifuging. Moreover, the salt content of any slight sediment obtained is so high as to preclude the ordinary precipitation test. He points out further that it cannot be said that these fluids in which the Wassermann was weakly positive, the precipitation test negative, and the protein content either normal or only slightly increased represent false positive Wassermann reactions, for three-fourths of these cases presented clinical evidence of central nervous system involvement. Eagle concludes that the Wassermann reaction remains the method of choice in the examination of spinal fluids. Until some method has been found of increasing the sensitivity of the precipitation tests in spinal fluids, the Wassermann test cannot be entirely replaced by precipitation tests, no matter how great their technical simplicity, reliability, or sensitivity with serum.

Davies (*19*) applied his modification of the Hinton test to the examination of 965 spinal fluid specimens on which the "Wassermann test" was also done. He stated that there was only one definitely false positive Hinton reaction, that there was disagreement between the tests in 63 cases, and that in 81 percent of these "the modified Hinton test was found to be correct." Since he does not explain this statement and offers no data on the clinical findings, the number of syphilitic and nonsyphilitic patients examined, and the number of patients known to have central nervous system syphilis, and since nothing is known of the Wassermann technic employed no conclusions can be drawn from this report.

Marquis (*80*) reported on a comparative study of the Davies-Hinton and the "Wassermann" tests of the spinal fiuid of 200 patients in 1939. However, he did not state what "Wassermann" technic was used and did not discuss his group of 79 patients with syphilis separately from the nonsyphilitic patients in evaluating the results. A comparative study of the Davies-Hinton and the Kolmer tests carried out in laboratories of high standing other than those of the originators would be of interest.

On the basis of all of the foregoing studies, it is apparent that one or even several official evaluation studies do not finally establish the compara-

tive value of any single test. The results of official evaluation studies are no doubt of great value but they cannot be said to be final. They have to be considered in the light of all that is known about the serologic diagnosis of syphilis.

REPORTING RESULTS AS POSITIVE, DOUBTFUL, AND NEGATIVE

The recommendation that plus marks be dropped in the reporting of serologic tests for syphilis, and that the words "positive," "doubtful," and "negative" be used instead, was first made at the League of Nations serologic conference at Copenhagen in 1923. This designation of results of tests was also used at the other conferences sponsored by the League of Nations and was later adopted by the American serologic conferences.

Moore (*91*) has pointed out that the reporting of results of serologic tests in terms of plus marks is inaccurate and misleading. He states that "four plus" does not necessarily mean "strongly positive," since all tests in current use are qualitative or only roughly quantitative, that is they are performed with a fixed amount of whole serum related to the total bulk of the test and ranging from 0.1 to 0.025 cc. A test may be positive with as little as 0.00005 cc. of whole serum. In such a case, if plus marks are to be used in reporting, the result might properly be expressed as "four thousand plus" instead of "four plus." He thinks it is obvious therefore that plus marks and the qualifying adjective "strongly" should be eliminated from routine serologic terminology and should be replaced by the single word "positive." He goes on to say that though "positive" covers an extreme range of variation in terms of the amount of patient's serum employed in the test, the other symbols, 3 plus, 2 plus, 1 plus, and plus-minus which are commonly used to describe a "partially positive" or "doubtful" result, cover instead an extremely minute range of variation, this range being only between the limits of 0.2 and 0.02 cc. of whole serum in the Wassermann test. Within this narrow range, there is no valid excuse for the attempt to report minute variations in the degree of positiveness and all such results should be expressed by the word "doubtful."

This advice sounds very logical and the solution ought to be simple except for the fact that there seems to be no generally accepted basis of the classification into positive, doubtful, and negative results. Kolmer (*69*) considers 3 plus reactions in his test as positive (4 plus as strongly positive) instead of doubtful as Moore would consider them. In the description of his technic Kahn (*124*) gives a definite basis on which to make the diagnoses of positive, doubtful, and negative. Whether this is followed by all laboratories using the Kahn test is another question. Binkley (*5*) reports that the Ohio State and Cleveland City Hall serologic laboratories consider 4,

3, and 2 plus as positive, 1 plus and plus-minus as doubtful, and minus as negative. And no doubt other laboratories to whom the classification positive, doubtful, and negative appeals will have their own ideas which number of plus signs to include under which of the three classifications, and the final result is that no one has got away from the plus signs at all. The only difference is that the physician is somewhat more muddled than before because formerly he could at least evaluate the plus signs as he saw fit; now two laboratories may report exactly the same result but one calls it strongly positive and the other calls it positive, or the one calls it positive and the other calls it doubtful.

Mahoney and Harrison (*78*) state that the recommendation in regard to the use of the terms positive, doubtful, and negative is probably the most helpful to the average physician. Many clinicians who are interested in the treatment of syphilis desire only the actual readings of the test. The method of the future probably lics between the two; that is, advising the physician of the actual readings together with the originator's interpretation of the degree of positivity shown.

Casselman (*114*) has pointed out that some index of the quantity of reagin in the blood in the doubtful zone is needed, whether this be indicated by hieroglyphics or by units, or whatever index. He says: "I wonder if there is an expert syphilologist who does not ask his technician in his own laboratory for more than a doubtful report in the doubtful zone. Of course, I am not suggesting in any way that we should not report doubtful, negative, and positive, but sometimes it is of value to have the additional information." This criticism of the inadequate evaluation of the doubtful zone has also been made by Wadsworth, as already pointed out.

It is absolutely necessary, if the classification positive, negative, doubtful is to be used that a definite and standard basis of classification be established. If this is done, this classification is undoubtedly superior to the old one, and for this reason: Physicians who are not serologists or syphilologists may consider a positive serologic test for syphilis to be concrete evidence that the person whose blood gives this reaction has syphilis. No matter how ultrasensitive the test or how few the positive plus signs, as long as the test reads "positive" the patient is considered to have at least a "slight" syphilitic infection. Misinformed physicians have therefore given antisyphilitic treatment to patients who had positive "screen tests" with the other tests being negative or who had plus-minus, 1 plus, and 2 plus reactions, especially if these reactions were confirmed by a repeat test. When such reactions, however, are not called "positive" but are reported to the physician as "doubtful" he will consider them as doubtful and not as positive and will be much less apt to diagnose syphilis and make haste to begin treatment on the basis of the test result alone.

UNITED STATES SEROLOGIC CONFERENCE OF 1938

In October 1938 a conference of laboratory directors and serologists was held under the auspices of the Committee on Evaluation of Serodiagnostic Tests for Syphilis and the U. S. Public Health Service at Hot Springs National Park, Ark. (*114*). At this conference Surgeon General Parran outlined the aims and purposes of the assembly as follows:

1. Adaptation of present efficient serologic tests as performed by the originators to the diverse and often unfavorable conditions existing in ordinary laboratory practice.

2. Improvement of test performance by encouraging adherence to conventional technic in laboratories too small or too greatly overworked to engage in intensive research studies.

3. Careful selection and thorough training of laboratory personnel. The country's best serologists have agreed to give special training courses. For this purpose additional funds have been made available. State health officers may, for example, use for training purposes Federal funds appropriated either under the Venereal Disease Control Act or the Social Security Act.

4. Organization of Nation-wide and State-wide studies to determine the efficiency of serologic test performance . . .

5. Investigation of the present need for approval or licensing of laboratories within a State by the State department of health, and recommendation of the methods to be followed if such licensing or approval is deemed advisable.

At this conference Mahoney and Harrison outlined the sources of error in the performance of serodiagnostic tests. Their criticisms were based on the results of the 1938 study by the Committee on the Evaluation of Serodiagnostic Tests. They found that errors were due to (a) the use of outmoded technics, (b) the modification of the originator's technic by the laboratory, (c) the use of short-cuts and time-saving devices, and (d) the inferior quality of essential ingredients, for example, the local production of antigens and their use without proper standardization and the use of inferior complement in the complement fixation reaction.

The committee recommended that all laboratories should closely adhere to the technic described by the originator of the test used. To make this possible, the originator should describe the technic of his method with the greatest accuracy and in detail and widely publish any improvements or changes which he makes in the technic. The committee recommended the publication, in complete detail, of the technical procedures to be observed in the performance of each of the reliable, evaluated serologic tests for syphilis now commonly employed in this country. They recommended that such publication should be issued by the U. S. Public Health Service in collaboration with the originators of reliable methods as a supplement to

Venereal Disease Information. It should be made available without cost as soon as possible to all laboratories performing serologic tests for syphilis. In order to insure adequate distribution, a census of central and branch State laboratories and municipal, hospital, and private laboratories should be made by the U. S. Public Health Service in cooperation with State health officers. This publication should be brought up to date and reissued at intervals of approximately 2 years, at the discretion of the Surgeon General. It was pointed out that periodic visits by consultant serologists to laboratories performing serologic tests for syphilis is so highly desirable that the committee recommended that steps be taken to make such consultation service available on request. By such person-to-person conference it is possible to make certain that the technic is understood in minute detail; deviations from approved methods may thus be detected and corrected and the sources of error eliminated.

Technicians performing serodiagnostic tests should have a good knowledge of the basic principles involved.

Hazen outlined the following classification of laboratories, based on their performances in the serologic evaluation:

1. Satisfactory laboratories are those which secure a specificity rating of 98 or 99 percent, depending on whether 100 or 200 samples are examined, and a sensitivity rating of not more than 20 percent below that of the control laboratory in cases of late or treated syphilis, and a rating within 1 percent of that of the control laboratory in cases of untreated secondary syphilis.

2. Laboratories which do not have the above rating shall be classed as unsatisfactory.

3. It is possible that a third group of laboratories should be considered, namely, those that are as good as or better than the control laboratories. This would require a specificity rating of 100 percent and a sensitivity rating at least equal to that of the control laboratory.

In regard to "screen tests," Hazen said that the employment of a very sensitive "screen test" may be justifiable in certain exceptionally well run laboratories as an economic procedure. All negative serums are at once discarded; all positive serums are put through a "battery" of tests in order to determine the proper report. It is to be remembered, however, that a "screen test" may give a negative result, whereas the other, less sensitive tests are positive. Undoubtedly, therefore, a certain percentage of positive serums will be overlooked by the use of this method but probably not more than 2 percent. Hazen recommends that every pregnant woman and every professional donor should be examined by both complement fixation and flocculation tests.

Recommendations were also made at this conference in regard to the details of the procedure which is to be followed by the various State health officers for State control-laboratories in the evaluation of the efficiency of

serologic testing as performed by the laboratories within the State. These recommendations which are lengthy will not be reviewed here. According to them a laboratory may qualify as satisfactory if it has a sensitivity rating which is not more than 10 percent below that of the State control-laboratory and a specificity rating of not less than 99 percent. It was advised that the efficiency of the laboratories be checked every 2 years.

The committee expressed itself as not in favor of State licensure but advocated a system of approval on a national basis. The following recommendations were made:

1. That the Surgeon General of the United States Public Health Service be requested to establish in the Public Health Service a Department [office] of Serology under a director, organized for fundamental research and for standardization of the reagents and procedures in the different serologic tests for syphilis and for the evaluation of the performance of serodiagnostic tests for syphilis. Provisions should be made in the future for distributing standards as is done so successfully in the case of therapeutic serums.

2. That the Surgeon General be requested to appoint a national advisory council on serology of representative experts whose duties shall be purely advisory to the Department [office] of Serology. A council of eight members is suggested with terms expiring so that two appointments or reappointments are made each year. The director of the Department [office] of Serology is to be a permanent member of the committee. The council may on request or on its own initiative express any opinion or submit recommendations as to policy or procedure that may serve to promote improvement of laboratory service in the diagnosis of syphilis in the United States.

3. That a national census of all laboratories doing serologic work, including those doing spinal fluid and dark-field examinations, should be made at once by the United States Public Health Service.

4. That laboratory service in the serologic and other aids to the diagnosis of syphilis throughout the United States be improved, extended and made more readily available:

a. By establishing standards for approval and approving laboratories that perform efficient tests. The director must be qualified for the position by training and special experience in the field and must assume responsibility for all of the examinations made in the laboratory and must determine if members of his staff are competent to perform the duties assigned to them.

b. All approved laboratories and all those who are seeking approval for the performance of serologic tests and dark-field and spinal fluid examinations should be offered inspection by and conference with qualified representatives of the Department [office] of Serology. . .

c. By the granting of subsidies, when necessary, to States to aid in the maintenance of properly qualified laboratories. The development of approved local laboratory service is of primary importance. . . All communities should have access to diagnostic laboratory service which will include those for the prompt examination of specimens of spinal fluid and for dark-field examinations.

5. That State and local appropriations be made sufficient to permit a laboratory to be conducted on a satisfactory basis including the performance of at least two different tests when necessary.

6. That when the United States Public Health Service is satisfied with the facilities offered by a State laboratory, approval but not necessarily licensure of local laboratories, should be undertaken by the individual State. In cities to which State sanitary codes or similar legislation do not apply, if the municipal laboratory has been found to be efficient, the municipality should undertake the supervision of its local laboratories. Otherwise the Public Health Service should cooperate with the State or large municipality in an effort to provide satisfactory facilities in such laboratories.

7. That the Surgeon General should withhold Federal grants-in-aid to State laboratories or the reallotment of Federal funds to local laboratories, if such laboratories are performing inefficient tests for syphilis and are not attempting to further the development of reliable local laboratory service . . .

8. That standards for evaluation of the efficiency of laboratories be adopted. [Approval should be renewable from year to year contingent on the maintenance of satisfactory work.]

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SYPHILIS in the Negro

A Handbook for the General Practitioner

by

H. H. HAZEN, M. D.

Professor of Dermatology and Syphilology

Howard University

Washington, D. C.

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Foreword

In the preparation of this book great assistance has been rendered by the permission of the Journal of Negro Education to use material from an article by the author, appearing in the July 1937 issue; and of the C. V. Mosby Company to utilize certain tables and passages of the author that have been published in the September 1936 issue of the American Journal of Syphilis, Gonorrhea and Venereal Diseases; and in addition certain other material from his second edition of Syphilis. Charles C. Thomas has likewise extended permission to reproduce tables from Dr. J. E. Moore's Modern Treatment of Syphilis.

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Introduction

The odds that the American Negro will acquire syphilis are so much higher than for the white individual that a casual observer might be inclined to identify the syphilis problem in the United States with the Negro race. He could point, off-hand, to any of the considerable mass of old and new data from North and South supporting Surgeon General Thomas Parran's statement (*1*) that syphilis occurs six times more frequently among Negroes than among whites.

Nevertheless, the casual observer's identification of the problem would be mistaken. True, even with careful study, one cannot escape the observation that the greatest single reservoir of syphilis in America is the Negro. But when one seeks an explanation through prevalence surveys in various areas where the Negro comprises a significant proportion of the population, he finds the problem transcends racial boundaries. Where the Negro syphilis rate is high the rate in the white group as well is likely to be unusually high. He finds, by comparison of these areas with those having lower rates for both Negro and white, that a less vigorous effort has been made to control the disease. Treatment facilities in the areas of high prevalence prove to have been inadequate and largely inaccessible. Likewise, the public is not well informed on the value of early and adequate treatment in arresting the disease and in preventing its spread. And he reaches the conclusion that the most outstanding characteristic of these areas of high prevalence is a low economic status in a large proportion of the population.

A 1939 study (*2*) of syphilis and gonorrhea under treatment in Washington, D. C., demonstrates the point. The venereal disease rate for individuals with annual incomes under $1,000 was 34.6 per 1,000 population compared to 6.4 for those in the $1,000–$3,000 income group and 4.7 for those earning more than $3,000. Table 1 shows an excess of syphilis in the lowest income group for both white and Negro groups, the inequality of distribution weighing more heavily in the white than in the Negro. Whereas the under-$1,000 class makes up only 18.6 percent of the white population, it contains 43 percent of the white syphilis population. The lowest income group makes up a much larger part of the Negro population—77.7 percent—and contains 86.6 percent of the syphilis population. In the higher income groups, white or Negro, the situation is reversed. Other similar studies have been made. One in Richmond in 1932 placed 70.4 percent of the venereal disease patients surveyed under the classification "poor," the percentage for white being 47.1 and for Negro 86.4. It has been observed (*3*, *4*, *5*) that Negroes in higher economic brackets, just as white persons, have much lower syphilis and other morbidity rates.

TABLE 1.—*Percentage distribution by income of general population and syphilis population in Washington, D. C., 1939*

Annual income	White		Negro	
	General population [1]	Syphilis population	General population [1]	Syphilis population
Under $1,000	18.6	43.0	77.7	86.6
$1,000–$2,999	65.7	45.0	21.6	13.0
Over $3,000	15.7	12.0	.7	.4
Total	100.0	100.0	100.0	100.0

[1] National Resources Committee, Consumer Incomes in the United States, Washington, 1938 Distribution for white population from table 22b—Large cities 100,000 to 1,500,000 population; for Negro population from table 21b—Large cities 100,000 population and over.

Despite the alliance of syphilis and poverty, syphilis has receded wherever the people have been informed of the methods of prevention, detection, and cure, and, meanwhile, provided with facilities for obtaining treatment irrespective of their financial status. In obtaining funds to create the necessary personnel and equipment for such a program, legislators find they can measure the problem and convince public opinion of it far better with factual statements than by rhetorical appeals. In an effort to provide a complete understanding, the facts and figures prepared have been broken down in some instances to show the racial distribution of syphilis. This procedure has been deprecated by those charged with the health of the Negro. Their objections are easy to understand. Employers are disinclined to hire persons with syphilis, especially as domestics and food handlers, although (*a*) the infection is seldom spread through indirect contacts and (*b*) the individual under regular and adequate treatment is noninfectious. The suppression of statistics giving specific rates for the white and Negro, however, is perhaps an evasion rather than a solution of the problem syphilis imposes upon the basic question of Negro unemployment. The disastrous impact of syphilis upon the individual's health and consequently upon his social and economic existence cannot be suppressed. Rejection for employment because of syphilis stands as a challenge to the Negro race.

The Negro's best answer to the consequences of syphilis is to get rid of the disease. How? By utilizing every means available to teach the infected population the advantage to the patient and to the community of seeking early treatment, and by making certain that complete information on the extent of the problem is placed before legislative bodies so that adequate preventive and control measures may be provided. Undoubtedly much can be gained by bringing public opinion to bear on the total preval-

ence rates in a given area, but much more can be done by emphasizing that the larger part of the problem lies in creating treatment facilities for those who cannot pay for medical care. It may be desirable that in future comparisons of high and low prevalence rates in various areas, economic rather than racial factors be taken as bases. This suggestion is made in the belief that it may present a better answer than one which tends to stigmatize a racial group.

Yet, if the Negro physician or civic leader wishes to shift from the defensive to the offensive in seeking to throw off the burden of syphilis upon his race, he must show his people that only by publication of comparative statistics can public attention be brought to the need of providing greater funds to combat syphilis in the Negro. It is the moral responsibility of these better privileged Negroes to make a heroic attempt to help their race wipe out its higher percentage of syphilis. Data showing this provide these leaders with arguments which cannot be denied. They enable the Negro leader to say to Congress, to the State legislature, and to State and local health departments:

> Here are the facts. Statistics show that our race has too much syphilis. We need more help than white people because a greater portion of our population live in economic conditions which aid and abet the spread of syphilis. Our young people acquire syphilis at an earlier age than whites, which means more of them are economically disabled before they have a chance to support themselves. We want better facilities for training Negro medical students. We want more hospitals and clinics and general facilities for adequate medical care, particularly in the South. We want representation on State and local boards of health. Our syphilis not only harms us but the whole population by decreasing its working efficiency and increasing its dependents. What we demand is to public advantage.

The Negro should capitalize on the prevalence of syphilis in his race. He should use his ammunition, not bury it.

Part I

Incidence, Prevalence, and Trend

Approaches to the Problem

Study of syphilis in the Negro involves a group of approximately 15,000,000 individuals in a total population of 131,000,000. The colored population comprises about 11 percent of the whole. Geographically, around 79 percent of the 15,000,000 are concentrated in the 17 Southern States where they comprise approximately 25 percent of the population. Another 18 percent is found in the 3 Middle Atlantic and 5 North Central States, making a total of 97 percent in these 25 States. About 90 percent of those living in the South are rural inhabitants in contrast to the urban concentration of 80 percent of those living in the North. The median age for all Negroes in the United States is 23 and there are 97 males for each 100 females.[1]

An adequate definition of the problem of syphilis in the Negro or, for that matter, in the white would include a statement of the total number of cases occurring annually in that population group. Unfortunately, such a statement is impossible. If syphilis were comparable to other epidemic diseases—such as typhoid fever, diphtheria, poliomyelitis, or even pneumonia and influenza—a fairly adequate statement would be possible on the basis of cases reported by private physicians and by clinics to State and local health departments. But syphilis has neither the comparatively violent onset nor short course typical of these diseases. The infection usually begins inconspicuously and proceeds slowly; hence it may slumber undetected in vast numbers of the syphilitic population. Then, due to its imitative quality, it may not be correctly diagnosed when it produces symptoms sufficiently alarming to send the patient to a physician. Finally, syphilis lacks the social respectability of other contagious diseases, with the result that public recording is avoided or disguised. In consequence, the number of cases reported to health departments fails not only as an index of the number of syphilitics in the population but also fails as an index of the number of cases under medical treatment. Only a fraction of syphilis in any group is known syphilis.

The United States Public Health Service and cooperating groups have constantly faced the difficulty of defining the total syphilis problem since the inception of the national syphilis control program. The limitations in their measuring sticks are the limitations in the amount of syphilis

[1] The median age for the white population is 27 and the ratio of males to females is 103 to 100.

detected in the population and the smaller amount reported. Nevertheless, the Public Health Service and cooperating clinics, health departments, and private physicians have been able to provide good indications (but only indications) of incidence and prevalence, principally by the following methods:

1. Surveys in selected communities and areas of the number of syphilis patients admitted for treatment each year by physicians, clinics, and hospitals. The number of patients divided by the survey population provides the discovery rate, as the term is used in this procedure. Likewise, the number of patients with early syphilis (i. e., primary, secondary, and latent syphilis of less than two years' duration) yield the attack rate, also called the incidence rate.

2. Surveys in selected communities and areas of the number of syphilis patients constantly under treatment, i. e., the average number regularly attended by the medical sources reporting. This number divided by the survey population gives the prevalence rate, as the term is used in this procedure. These methods of incidence and prevalence study were at first carried out among cooperating sources by circulation of questionnaires, telephone calls, and personal visits until sufficient data were abstracted for manual tabulation. Now, however, a system of mechanical accounting known as the central tabulating unit (*6*) has been installed in 12 cities to provide regular and uniform morbidity reports for all participating clinics. These units serve more than 1,000 clinics in 25 areas (States, counties, and cities). The morbidity reports not only measure the early and late syphilis in the clinic population, but progress in antisyphilis treatment, case-finding, and case-holding.

3. Tabulation and combination of the syphilis cases reported each year by State departments of health. This provides an annual discovery rate by States and for the United States.

4. Serologic surveys of selected communities and areas, in which blood tests for syphilis are made on all volunteers. Insofar as the sample is statistically adequate and representative of the survey population by age, sex, race, and income, the serologic survey supplies a more effective measuring stick of the true prevalence of syphilis because the hidden reservoir of the disease in the general population is tapped. The accuracy of the serologic survey, of course, depends upon the efficiency of the serologic test as well as upon the representativeness of the survey group. Performed by competent laboratories, the standard serologic technics are 98 or 99 percent specific in the validity of positive reactions obtained and from 70 to 80 percent sensitive in detecting known syphilis (*7*). In addition, the serologic test misses the seronegative primary case. But the losses through serologic inefficiency in this dragnet system are considered negligible.

The discussion of incidence, prevalence, and trend will be confined for the most part to facts revealed by the above methods of survey which are all, it should be remembered, less than total statements of the problem.

The United States Public Health Service estimates that more than a half million (518,000) new syphilis infections occur in this country each year (*8*). This estimate is based on a study of early syphilis reported under treatment by cooperating physicians and clinics between 1927 and 1933 in 34 communities with a total population of 14,000,000. The attack rate was 4.1 per 1,000 in a total annual discovery rate of 8.4. No color breakdown was possible in this sample. In a smaller sample—29 communities with a population of 5,500,000—the following comparison of white and colored discovery rates was made.

TABLE 2.—*Annual discovery rates per 1,000 population for syphilis in 29 communities, 1927–33*

Syphilis	Males			Females			Total		
	White	Colored	Total	White	Colored	Total	White	Colored	Total
Early	8.4	16.0	9.5	3.3	9.1	4.1	5.9	12.6	6.8
Late	5.5	18.4	7.2	3.1	14.6	4.7	4.2	16.5	6.0
Total	13.9	34.4	16.7	6.4	23.7	8.8	10.1	29.0	12.8

The above study shows a 2-to-1 greater frequency in the attack of syphilis on the colored group compared to the white, a 4-to-1 ratio in the rate at which colored and white patients are admitted annually for treatment of late syphilis, and a 3-to-1 ratio in the discovery of both early and late syphilis in the colored group. While males of both races have more syphilis than females, the difference between colored male and female rates is less pronounced. The difficulty of discovering early infections among women probably accounts for the higher number of first admissions to treatment for males.

A new study of the influence of color on the number of patients seeking antisyphilitic treatment each year has been made by the United States Public Health Service, and is published here for the first time. The study combines 41,000 cases under treatment between 1933 and 1939 in 22 cities and 5 rural areas with a total population of 7,600,000. Table 3 shows an attack rate of 1.5 per 1,000 population for both white and colored and a total annual discovery rate of 5.4. It is immediately seen that the attack rate is three times as high in the city as in the country for whites and twice as high for Negroes, with the same or greater differences in late syphilis. This may be attributed to some extent to the greater opportunity for exposure presented by the closer environment of city life, but Usilton (*8*) found that the disparity of rates is largely the result of rural patients being forced to seek treatment in urban clinics.

TABLE 3.—*The influence of color of patient on the annual discovery rate for syphilis in 22 cities and 5 rural areas of the United States.*

City or rural area	Total estimated population	Percent colored	Case rate per 1,000 population								
			Early or acute			Late or chronic			Combined totals		
			White	Colored	Total	White	Colored	Total	White	Colored	Total
Chicago, Ill	3,258,569	7.3	0.5	4.8	0.8	2.3	25.3	4.0	2.8	30.2	4.7
Cleveland, Ohio	1,112,072	6.6	2.8	7.2	3.1	2.6	16.2	3.5	5.4	23.4	6.6
Baltimore, Md	855,127	19.5	.7	5.9	1.7	1.5	18.5	4.8	2.2	24.5	6.5
Washington, D. C	627,000	27.2	.8	5.7	2.3	1.9	23.9	7.9	2.7	29.5	10.0
Omaha, Nebr	214,006	5.2	1.8	4.6	1.9	2.4	12.7	2.9	4.2	17.3	4.8
Richmond, Va	182,859	29.0	3.2	11.3	5.6	2.7	17.4	7.0	5.9	28.8	12.5
Wichita, Kans	111,110	5.1	1.5	3.7	1.8	2.0	5.9	2.2	3.4	9.6	3.7
Lansing, Mich	84,487	1.8	1.4	15.9	1.7	3.7	12.6	3.8	5.1	28.5	5.5
Lincoln, Nebr	75,933	1.3	.4	3.0	.5	2.1	30.1	2.5	2.6	33.1	3.0
Topeka, Kans	64,120	9.0	1.9	4.2	2.1	1.9	3.1	2.0	3.8	7.3	4.1
Hutchinson, Kans	27,085	3.5	1.3	3.1	1.3	1.7	3.1	1.8	3.0	6.3	3.1
Salina, Kans	20,155	2.6	.5	0	.3	.5	0	.4	.9	0	.9
Grand Island, Nebr	18,041	.7	.5	0	.5	1.7	0	1.7	2.2	0	2.2
Emporia, Kans	14,067	4.0	.7	0	.7	.7	5.3	.9	1.3	5.3	1.5
Lawrence, Kans	13,726	10.5	2.2	2.1	2.2	1.2	6.3	1.7	3.4	8.4	3.9
N. Platte, Nebr	12,061	.3	2.2	85.7	2.5	2.2	257.1	3.0	4.5	342.9	5.5
Freemont, Nebr	11,407	.5	.8	0	.8	.8	0	.8	1.6	0	1.6
Newton, Kans	11,034	4.7	.3	0	.3	.9	5.8	1.1	1.1	5.8	1.4
Norfolk, Nebr	10,717	.3	1.1	0	1.1	2.0	0	2.0	3.1	0	3.1
Eldorado, Kans	10,311	2.2	.9	0	.9	1.5	13.4	1.7	2.4	13.4	2.6
Beatrice, Nebr	10,297	.8	.3	0	.3	1.2	0	1.2	1.5	0	1.5
Manhattan, Kans	10,136	3.3	.3	0	1.3	.9	9.0	1.2	1.2	9.0	1.5
Total urban	6,754,320	10.8	1.1	6.0	1.6	2.2	21.3	4.3	3.3	27.3	5.9
Kansas [1] (all counties)	336,336	1.4	.2	.6	.2	.2	3.8	.3	.4	4.5	.5
Maryland (5 counties)	310,091	12.4	.3	4.4	.8	.3	2.6	.5	.6	7.0	1.3
Nebraska [1] (all counties)	131,555	.2	.5	0	.5	.3	0	.3	.8	0	.8
Michigan (Ingham county)	34,044	.2	.9	107.1	1.1	2.4	89.3	2.5	3.2	196.4	3.6
Georgia (3 counties)	31,491	50.5	1.2	.9	1.0	4.4	30.5	17.6	5.5	31.5	18.7
Total rural	843,517	7.1	.3	3.2	.5	.4	10.2	1.1	.7	13.5	1.6
Grand total	7,597,837	10.4	1.0	5.8	1.5	2.0	20.5	3.8	3.0	26.2	5.4

[1] Exclusive of cities of more than 10,000 listed above.

The ratios between white and colored and between male and female in the new study may be judged from the rates given in table 4.

The total rates are much lower than in the previous study except for late syphilis in the colored which is increased by the colored females. But the frequency ratios between colored and white are much higher. Six colored persons have early syphilis for every 1 white in each 1,000. The frequency of late syphilis among the colored group is 10 times greater. The frequency ratio for both early and late syphilis is almost 9 to 1. In both old and new studies the white-colored ratios were about twice as large for late as for early syphilis, indicating perhaps that Negroes have had less impetus and

less opportunity to seek treatment during the infectious early stages of the disease when chances both for control and for cure are the best.

Comparisons and conclusions must be made cautiously, however, since neither study is regarded as entirely representative of the problem in the general population. Moreover, the geographic groups studied do not correspond. The old study inclined more to the South and to the urban than the later one. The possible effect of control measures intervening between the two studies will be discussed under "Trend."

TABLE 4.—*Annual discovery rates per 1,000 population in 22 cities and 5 rural areas, 1933–1939.*

Syphilis	Males			Females			Total		
	White	Colored	Total	White	Colored	Total	White	Colored	Total
Early	1.3	6.5	1.9	0.6	5.0	1.1	1.0	5.8	1.5
Late	2.5	18.4	4.1	1.6	22.5	3.8	2.0	20.5	3.8
Total	3.8	24.9	5.9	2.2	27.4	4.9	3.0	26.2	5.4

PREVALENCE

"Syphilis strikes 1 out of 10 adults." This statement, originated by Dr. Parran, has become one of the most popular statements of syphilis prevalence, although it actually refers to incidence. From it, many people have got the idea that 10 percent of the population have syphilis at any time; the figure is more likely about a tenth of that. The statement means that 1 of every 10 adults will acquire syphilis sometime during his life (*9*). Of 100,000 persons aged 15 without syphilis, 10,000 will have syphilis by the time they are 50 years old. The chance of acquiring syphilis during life has not been estimated for white and colored groups separately, but it is apparent that it must be much higher in the colored population because (*a*) more Negroes have syphilis, (*b*) they acquire syphilis at an earlier age, and (*c*) their life expectancy is considerably less.

The first point has already been demonstrated.

The second point is borne out by a United States Public Health Service study, published herewith in table 5, of the percentage distribution by race, age, and sex of 11,258 cases of early syphilis receiving treatment for the first time in medical sources representing a survey population of 11,429,000. Syphilis begins its sharp attack on the colored group in the 15–19 age group and reaches its peak of new infections between the ages of 20 and 24, while in the white group the upward surge begins in the 20–24 group and reaches a crest in the years 25–29. From this table it may be seen, in addition, that 76.8 percent of all new infections among Negroes occur between the ages of 15 and 30 compared to 59.5 percent in the 15–30

white group. Further, two-thirds of Negro women with early syphilis acquire the disease before they are 25 whereas but half of the men are infected before that age.

The third point is established by 1929–31 figures (*10*) showing a life expectation at birth of 47.52 years for colored males and of 49.53 for colored females compared to 59.31 and 62.83 years, respectively, for white males and females. The same source attributes the excess of the annual Negro death rate over the white (18.0 as against 9.9 per 1,000 in 1930) largely to syphilis. Another study (*11*) places the life expectancy for infected Negro males between the ages of 30 and 60 at 30.5 percent less than for the average man of his race compared to a loss of 17.3 percent for white males of like age.

TABLE 5.—*Distribution per 100 by sex and age of 11,258 Negro and white patients in a survey population of 11,429,000 receiving treatment the first time for early syphilis*

Age	Negro			White			Total		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
Under 15	1.4	2.9	2.1	1.4	1.1	1.3	1.4	2.0	1.7
15–19	14.9	29.3	21.9	6.4	12.8	8.9	9.7	20.7	14.4
20–24	34.1	33.5	33.8	21.7	28.5	24.4	26.5	30.9	28.4
25–29	22.6	19.6	21.1	24.6	28.5	26.1	23.8	24.2	24.0
30–34	12.6	8.4	10.6	16.7	11.7	14.7	15.1	10.1	13.0
35–44	9.1	6.3	7.7	20.9	15.6	18.9	16.4	11.2	14.7
45 and over	5.3	0.0	2.7	8.1	1.8	5.7	7.1	0.9	4.5
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

In 1935 the United States Public Health Service found that the prevalence of syphilis (i. e., the number of patients constantly under treatment) is 4.3 per 1,000 (*8*). The rate was derived from a study of 124,000 cases under treatment in a survey population of 29,000,000. From this it was estimated that 683,000 persons are under medical care for syphilis in the United States at any one time. No color breakdown was possible. While the number of cases generally reported has increased in the last 4 years (see table 14), no new study of comparable scope and more definitive nature has been made as yet. Thus, we can point to the greater proportion of Negroes in fragmentary studies, but cannot adequately answer the question: Of all known persons with syphilis in the country, how many are Negroes?

The best indication of which I know is the study of 41,000 cases in a survey population of 7,600,000 cited in the incidence discussion. Table 6 shows that 20,400 or 49.6 percent of the total cases were white and 20,600 or 50.4 percent were colored. The percentage of Negroes in the study was in keeping with the general population composition (8 white to 1 colored).

If the sample were representative, and this is not believed to be wholly the case, half of all syphilis under medical care in this country is Negro. The 6-to-1 frequency ratio in the attack rate, is well supported by other sources. For example, the Surgeon General of the United States Army reported 130 admissions to treatment per 1,000 colored troops and 19 per 1,000 white troops in 1918—a ratio of about 7 to 1. For the entire World War period, colored admissions were 64.9 per 1,000 compared to 12.6 per 1,000 white troops—a ratio of about 5 to 1. If the 6-to-1 frequency holds for the general population, 40 percent of all new syphilis strikes in a group comprising 11 percent of the population.

TABLE 6.—*Influence of color on distribution of early and late syphilis cases brought to treatment for the first time each year in 22 cities and 5 rural areas of the United States*

	White		Negro		Total	
	Number	Percent	Number	Percent	Number	Percent
Survey population	6, 807, 562	89. 6	789, 275	10. 4	7, 597, 837	100. 0
Survey cases	20, 421	49. 6	20, 698	50. 4	41, 110	100. 0
Early syphilis	6, 718	59. 6	4, 555	40. 4	11, 273	100. 0
Late syphilis	13, 703	46. 0	16, 143	54. 0	29, 846	100. 0

Prevalence rates based on cases constantly under treatment are absolute minimum statements of the problem. This is due to the patients' frequent failure to seek treatment until their infections are several years old, to clinical failure to keep known syphilitics under treatment, and to the failure of many physicians to report cases which do come under treatment. Thus, the serologic survey offers considerably more insight into the total problem.

The first extensive serologic survey made in the United States was the "Wassermann dragnet" conducted by the United States Public Health Service under a grant from the Rosenwald fund (*12*). A total of 27,131 Negroes were tested in 6 Southern counties between 1929 and 1932 with the results shown in table 7.

TABLE 7.—*Rosenwald serologic survey—1929–32*

County	Number examined	Percent positive
Macon, Ala	3,363	35.0
Glynn, Ga	5, 674	26. 9
Tipton, Tenn	2, 339	25. 9
Bolivar, Miss	2, 304	23. 6
Pitt, N. C	10, 198	11. 8
Albemarle, Va	3, 253	7. 1
Total	27, 131	19. 5

An unpublished serologic survey made in Albemarle County during a 2-year period ending in June 1940, established that 6.3 percent of the 3,132 Negroes tested had positive reactions. This is an 11-percent decline from the rate in the 1932 Rosenwald study, but when the old and new studies are adjusted by age and sex to the general population's composition the gain is seen to be much larger (see table 10). The new study included 3,284 whites. Their positive percentage of 1.1 is approximately one-sixth of the colored rate.

Other spot surveys have been made, but by far the most extensive is the blood-testing program which has been carried on since 1937 in Chicago, where Negroes comprise only 7 percent of the total population. In the 2-year period ending July 1, 1940, nearly 700,000 serologic specimens were submitted for syphilis diagnosis to the municipal laboratory alone (*13*). Of this number, 428,000 were from nonmedical sources without a clinical index of suspicion (public blood testing stations, field testing in schools and in industries, and premarital examinations). Table 8 shows that the 65,182 Negroes tested had a positive rate of 10.9 percent compared to 1.4 for the 362,897 whites tested. This is a ratio of about 8 to 1.

TABLE 8.—*Chicago serologic study, 1938–40*

	Number tested	Percent positive		Number tested	Percent positive
White	362, 897	1. 4	Colored	65, 182	10. 9
Male	221, 207	1. 6	Male	32, 239	11. 5
Female	141, 690	1. 1	Female	32, 943	10. 3
			Total	428, 079	2. 8

PREVALENCE OF CONGENITAL SYPHILIS

We have seen in the incidence and prevalence statistics given that syphilis acquired between the ages of 15 and 30 accounts for the major part of the rates. The amount of syphilis acquired *venereally* before the age of 15 is insignificant. Nevertheless, as table 5 shows, 1.7 percent of the cases in syphilis population may be found in children under 15. It is not much, but it is important. Practically all of it results from one of the most disastrous forms of the disease—congenital syphilis.

The problem of the syphilitic mother infecting the fetus may be judged from this statement:

Approximately 1 million of the potential mothers of this country have syphilis, and studies have shown that in a group of women who had never received antisyphilitic treatment only 17 percent of the known conceptions resulted in living nonsyphilitic children. The remaining 83 percent terminated in miscarriages, stillbirths, or living children with

syphilis. Each year these women with syphilis transmit the disease to at least 85,000 fetuses of which approximately 25,000 die before birth and 60,000 are born alive with syphilis (*14*).

What part of the 60,000 are Negro may only be guessed, but the distribution of the 25,000 syphilitic stillbirths has been estimated (*15*). Negroes contribute nearly 11,000 or 45 percent. Syphilis causes 19 percent of fetal deaths in the Negro compared to 7.4 in the white, according to the estimate.

A classical study of the affects of syphilis on childbirth (*16*) showed that syphilis is the greatest cause of fetal death. Among 302 intrauterine deaths in 4,000 deliveries, syphilis was responsible for 12.1 percent in the white and 45.2 in the Negro groups. The percentage of positive blood tests among the 4,000 women was 2.4 for white and 16.2 for colored.

Existing data for the true prevalence and incidence of congenital syphilis are even more fragmentary than the figures for all syphilis. The Rosenwald demonstration treated 5,905 Negroes for syphilis (*12*). The percentage of congenital syphilis among them was 14, while the percentage for the total group examined was 2.5. There was no basis for comparison of Negro and white. Nor is such a comparison available in the 3.4 percent of congenital syphilitics found among 10,000 consecutive admissions to the Johns Hopkins Hospital syphilis clinic (*17*).

Such a comparison is possible, however, in two surveys made in Chicago. The 1937 study (*18*) revealed that of the 10,484 white and 7,356 colored cases surveyed, 1,719 were diagnosed as congenital syphilis. The white group contained 7.8 percent congenital syphilitics and the Negro group 4.8 percent. Table 9 shows that the same greater proportion of congenital syphilis among white cases prevailed in the 1939 study (*19*) despite a reverse in the proportion of the white and Negro case loads. Now, with 7,975 white and 9,686 Negro cases under treatment and 759 classified as congenital, congenital syphilis made up 5.2 percent of the white cases and 3.6 of the Negro cases. Of course, when an incidence rate is calculated on the basis of population, the Negro rate becomes excessive. The frequency is 11.5 to 1.

TABLE 9.—*Annual incidence of early and late congenital syphilis in Chicago, 1939*

	Number of cases			Rates per 10,000 population		
	White	Colored	Total	White	Colored	Total
All syphilis	7,975	9,686	17,661	23.8	389.3	49.0
Congenital syphilis	413	346	759	1.2	13.9	2.1
Early [1]	51	42	93	3.5	38.4	5.7
Late [2]	362	304	666	1.1	12.8	1.9

[1] Patients under 3 years old. [2] Patients 3 years and older.

Trend

There is abundant evidence that syphilis in the Negro can be controlled once the effort is made.

Albemarle County is an excellent example. The comparatively low rate of positive bloods found among the county's 10,000 or more Negroes in the Rosenwald survey reflected the high character of this group and the control activity already instituted by the University of Virginia Medical School at Charlottesville, the county seat (*12*). Even so, considerable progress has been shown since 1932. In 1939, 3 years after the advent of the national syphilis control program, a serologic resurvey was made (*20*). Table 10 compares the adjusted case rates per 1,000 population on the basis of the first and second serologic surveys. The 1932 rate for colored males was 110 per 1,000 population and the 1939 rate 64.4—a drop of 41.5 percent. Likewise, the rate for colored females declined from 120 to 89.9 per 1,000, a reduction of 25.1 percent. A spectacular 100-percent decrease is shown among children under 10 years old. Rates of 31.8 and 44.0 per 1,000 for males and females respectively were calculated for 1932 whereas the 342 children in the 1939 sample yielded no positive blood tests. The next greatest gain was in the important 10-to-20 age group, the rate for both sexes declining more than 60 percent.

One of every five Negroes had syphilis in the combined areas at the beginning of the Rosenwald syphilis control demonstration. In general, the percentage infected reflected the economic and educational status of the six groups and the availability of medical care, Macon County having a predominantly rural colored population in which illiteracy is high and the standard of living very low. Albemarle's low rate, in contrast, reflected a relatively high socioeconomic status and good treatment facilities supplied by the University of Virginia's venereal disease clinic.

Table 10.—*Potential case rate per 1,000 population on the basis of serologic surveys among Negroes of Albemarle County, Va., 1931–32 and 1938–39, by age and sex* [1]

Age	Male			Female		
	1931–32	1938–39	Percent change	1931–32	1938–39	Percent change
0–9 years	31.8	0	−100.0	44.0	0	−100.0
10–19 years	36.4	11.5	−68.4	59.2	23.1	−61.0
20–29 years	146.9	87.7	−40.3	252.1	206.3	−18.2
30–39 years	238.5	138.7	−41.9	185.0	162.0	−12.4
40–49 years	174.8	115.6	−33.9	133.4	80.0	−40.0
50 years and over	111.0	97.7	−12.0	81.8	114.9	+40.5
All ages	110.0	64.4	−41.5	120.0	89.9	−25.1

[1] From the chapter, Venereal Disease Control in the United States, by R. C. Tumbleson, in "Health of the Negro in the United States," to be published by the Carnegie Foundation.

While such definitive comparisons of rates are not possible as yet in the other 5 areas of the Rosenwald demonstration, there are many convincing indications. In 1934 a resurvey was made in the Virginia, North Carolina, and Alabama Rosenwald survey areas to measure the effectiveness of the mass treatment program (*27*). The health of 1,345 individuals previously treated, expenditure of funds for recognized medical care or patent medicine, and opinion of both employers and individuals treated were factors studied.

It was found that those in poor health had dropped from 39 percent of the individuals before the demonstrations to 4 percent after the demonstrations. The improvement in general health was better reflected in the fact that while 40 percent of the patients before the demonstration were unable to do a full day's work only 7 percent indicated their inability after the demonstration. These individuals for the most part had been inadequately treated according to the modern standard. Seventy-five percent of them had received less than 20 doses of arsphenamine and interim heavy metal. There was a very noticeable decrease in the average cost of medical care. In North Carolina the average doctor's bill per syphilitic individual had dropped from $10 to $2, whereas in Alabama the cost had dropped from $12 to $3. The cost for patent medicine had also dropped proportionately from $4 to $2 in North Carolina, and from $3 to $2 in Alabama.

The opinion of the patient that the treatment had benefited him was practically unanimous, and there was a generally expressed desire to have more of this type of treatment made available.

In the survey territory most of the Negroes are laborers on various plantations. Most of the planters assume responsibility for the health of their employees, the cost of medical care being borne by the former. The planters stated that the average cost per employee of medical care had dropped from $18 to $7 in North Carolina and from $4 to $1 in Alabama. In practically every instance the planter was very enthusiastic about the results of the demonstration. It was further stated that some of the white laborers should be permitted to benefit in these projects.

The Rosenwald demonstrations proved the practicability of administering modern treatment for syphilis en masse in rural districts where improved facilities were not available.

Other fragmentary reports have been made of gains in the Rosenwald areas. "In 1930 the Glynn County stillbirth rate was 146 per 1,000 live births; in 1939, the rate had dropped to 65 per 1,000 live births, a decline of 55 percent. At the present time 90 percent of the Negro women of the county attend prenatal clinics before the fourth month of pregnancy. Local midwives are trained to bring expectant mothers into the health department for a blood test so that antisyphilitic treatment may be started as soon as possible during pregnancy. All infected workers in Glynn County are required to take routine treatment.

"A third survey area, Pitt County, N. C., revealed a positive rate in the marriageable age group of about 17 to 20 percent in 1930. Routine

premarital tests taken in 1939 over a significantly large group indicates that this rate has been cut in half during the intervening period of years (*20*)."

Comparison of the 1937 and 1939 Chicago surveys is also revealing (*18*, *19*). Reflecting intensification of case-finding activity beginning in 1937, the number of syphilis patients constantly under treatment by physicians and clinics increased from 14,349 in 1937 to 18,481 in 1939. The ratio of white to Negro in the total case load shifted from 3 to 2 to 5 to 6, as discussed on page 13. While the great gain in Negro cases increased the frequency of Negro syphilis compared to white from 8.5 to 1 to 17 to 1 on a population basis, the comparison is actually favorable to the Negro. It indicates a greater responsiveness among this group to blood-testing and treatment activities and hence definite progress in Chicago against syphilis in the Negro. The indication is borne out in other ways.

A study of the number of cases under treatment in Chicago in comparison to the potential case load indicated by the serologic survey conducted simultaneously leads to the conclusion that about 30 percent of the Negro potential case load is under treatment compared to only 13 percent of the white (*19*). This is shown in table 11, which also discloses that the average Negro patient remains under treatment as faithfully as the average white. This supports the opinion of many clinicians that the Negro is a willing patient once he is instructed properly.

The cooperativeness of the Negro is demonstrated further in Wenger's report (*13*). During a 2-year period 92 percent of Chicago's Negro males from 21 to 31 years old submitted to blood tests compared to only 31 percent of the white males in the same age group. For all ages and both sexes, the percentage of the general population receiving diagnostic serologic tests was 8.7 for white and 25.8 for Negro in 1940. Meanwhile 64.4 percent of the Negroes found to have syphilis through routine tests were brought under medical care, compared to 54 percent of the white group.

TABLE 11.—*Potential case rate, actual case rate, percentage of potential case rate under treatment, and average duration of treatment for Chicago patients (1939) by sex and color*

	Potential case rate per 1,000	Actual case rate per 1,000	Percent of potential rate under treatment	Average duration of treatment in months
White:				
Male	18.6	2.8	15.1	11.2
Female	18.7	2.1	11.2	14.8
Negro:				
Male	134.8	37.0	27.4	13.3
Female	142.1	45.2	31.8	12.2

A general decline in the percentage of positives found in the Chicago serologic survey was noted from 1939 to 1940. This is shown in tables 12 and 13. The decrease held not only in a sample of 700,000 consisting largely of routine tests made by physicians and clinics, where the index of suspicion is considerably higher, but in 58,000 tests made on couples applying for marriage licenses, a group which might be expected to approximate the general situation among young men and women. In the larger group, the white rate declined 0.8 percent from 2.9 to 2.1, and the Negro rate dropped 4 percent from 18.9 to 14.9. In the premarital group the white rate dropped 0.6 percent from 1.4 to 0.8 while the Negro rate dropped 3.6 from 10.4 to 6.8. The latter comparison seems particularly significant of a lessened prevalence of syphilis.

TABLE 12.—*Number tested and percentage of positives in Chicago serologic survey, 1939 and 1940*

	1939		1940		
	Number tested	Percent positive	Number tested	Percent positive	Percent decrease
White	279, 739	3. 2	261, 506	2. 4	—0. 8
Males	160, 670	3. 4	150, 241	2. 6	—. 8
Females	119, 069	2. 9	111, 265	2. 1	—. 8
Negro	91, 954	18. 9	65, 427	14. 9	—4. 0
Males	46, 688	17. 8	31, 762	14. 8	—3. 0
Females	45, 266	19. 9	33, 665	14. 9	—5. 0
Combined	371, 693	7. 0	326, 933	4. 9	—2. 1

TABLE 13.—*Number given premarital tests for syphilis and percentage of positives in Chicago 1939 and 1940*

	1939		1940		Percent decrease
	Number tested	Percent positive	Number tested	Percent positive	
White	22, 290	1. 4	27, 305	0. 8	—0. 6
Colored	3, 811	10. 4	4, 822	6. 8	—3. 6
Total	26, 101	2. 7	32, 127	1. 7	—1. 0

While there is no means of determining the Nation-wide trend in the prevalence of syphilis, United States Public Health Service records of control activities in the last 3 years are indicative of advancement in case-

finding and case-holding. Table 14 shows the great expansion in machinery to control syphilis.

The growth in the organization for case-finding is shown in the nearly 100-percent increase in number of blood tests for syphilis from 1939 to 1940. While the syphilis case-load remained fairly constant following the intensive case-finding in 1937 and 1938, the amount of arsphenamine distributed increased more than 300 percent over a 4-year period. The doubling of the number of clinics during the same period is significant of the attempt to make diagnostic and treatment facilities accessible to all sections of the population. Solution of this problem has advanced to the point where mobile clinics go to the rural patients in 21 counties in 8 Southern States.

TABLE 14.—*Annual number of syphilis cases under treatment, serologic tests, doses of arsphenamine distributed, and clinics in operation reported by 48 State health departments*

Fiscal year	Syphilis cases	Serologic tests	Doses of arsphenamine	Clinics operating
1937	366, 258	2, 618, 159	1, 567, 348	[1] 1, 380
1938	480, 140	3, 598, 198	2, 799, 110	1, 746
1939	485, 967	5, 588, 285	4, 677, 285	2, 405
1940	487, 464	10, 216, 978	6, 895, 837	2, 887

[1] Estimated, this data being unavailable.

Part II

Pathology and Clinical Course

Nature, General Effects, and Transmission of Organism

Syphilis is a chronic infection caused by a spirochete known as *Spirochaeta pallida* or *Treponema pallidum* (Figure 1, page 83). Schaudinn and Hoffmann discovered the organism in March 1905. It is spiral in shape, about 4 to 20 microns in length (approximately the diameter of a red blood cell), and persistently holds its tightly coiled form. It has two basic motions, one of boring and one of lashing. The lashing is characterized by sharp angulation.

Little of the life history of the syphilis spirochete is known. We cannot say whether the spirochete as we know it is the only form or just one form in a complicated life cycle. Cultures of the organism are not virulent. It is best kept alive by inoculating it into the testicles of a rabbit, an animal susceptible to the infection. Still unproved is the theory that there are different strains of *Spirochaeta pallida*, possibly with varying affinities for certain portions of the host.

The organism cannot withstand drying. It is easily killed by many antiseptics, weak solutions of any of the arsphenamines devitalizing the organism at once (*22*). It has poor resistance to heat or cold. Soap, also, kills it, thus providing reasonable security if the hands are washed thoroughly after treating or examining patients.

The spirochete can gain entrance to the body through the broken or unbroken skin or mucous membrane. It multiplies rapidly at the point of entrance and, following an incubation period usually of 3 to 4 weeks, commonly produces a chancre or initial lesion on the site of infection. But at least a week before the chancre is evident spirochetes may have spread to the neighboring lymph nodes, the spleen, bone marrow, and various other structures. For this reason, excision of a new chancre cannot be considered curative.

The chancre is known as the primary stage. From 3 to 8 weeks after its appearance, ordinarily about 4 weeks, there appear signs of a generalized infection known as the secondary stage. This consists of a widespread skin eruption, general enlargement of the lymph nodes, possibly sore throat, headache, fleeting joint pains, and sometimes other general symptoms. The skin, mucous membranes, blood, and secretions are capable of trans-

mitting the disease at this time. The external manifestations of this stage may continue for 3 months but will usually subside spontaneously.

Following the secondary period is the latent period, during which there is no overt trouble. This stage, which is insidious because serious lesions may be developing internally, may continue for varying periods from a few months to 20 or more years.

Late or tertiary manifestations may follow this period. In general, they consist of lesions of a destructive type which may occur in almost any organ or tissue of the body.

It is a general belief that the body has some resistance to the organism of syphilis, but again we are ignorant of the form of this immunity. Some individuals have so little defensive capacity against syphilis that it becomes malignant and from the onset produces ulcerous lesions frequently resulting in grave deformities. Others are affected little. Even the dreaded neurosyphilis may "burn out" in some persons, possibly leaving a few changes in the reflexes but no other apparent change.

The following classification of the stages of syphilis was formulated by the League of Nations and has been adopted by the United States Public Health Service:

S1. Primary syphilis (dark-field positive) with negative blood serum reaction on admission.

S2. Serodiagnostic positive primary syphilis.

S3. Secondary manifestations in first year of the disease.

S4. Secondary manifestations later than first year of the disease (recurrent secondaries).

Types of S3 and S4

a. Macular, except leukoderma.
b. Leukoderma.
c. Papular.
d. Pustular.
e. Follicular.
f. Annular.
g. Recurrent.
h. Mucous patches.
i. Condyloma.
j. Alopecia.
k. Leukoplakia
l. Visceral involvement (specify viscus).
m. Eye involvement.
n. Central nervous system involvement (specify type).
o. Others (specify).

S5. Latent (less than 4 years since infection). Latent comprises those cases which on admission have no other clinical or laboratory manifestation of syphilis except a positive Wassermann. If a spinal fluid test has been made it must be negative to have the case included in this group.

S6. Tertiary, all later, viz:

a. Tertiary with skin and mucous membrane lesions—

1. Nodular.
2. Gummous.
3. Nasopharyngeal.
4. Laryngeal.
5. Lingual.

b. Tertiary with visceral disease (except cardiovascular)—

1. Hepatic.
2. Gastric.
3. Nephritic.
4. Pulmonary.
5. Testicular and epididymitic.

c. Tertiary with cardiovascular syphilis—

1. Aortitis.
2. Aortic regurgitation.
3. Myocarditis.
4. Coronary sclerosis.
5. Aneurysm (specify location).
6. Myocardial failure.

d. Tertiary with bone and joint disease (specify location).

e. Tabes dorsalis.

f. General paralysis.

g. Central nervous system (other than e. and f.)—

1. Asymptomatic.
2. Meningeal.
3. Vascular neurosyphilis.
4. Meningovascular.
5. Optic atrophy.
6. Other (specify).

h and i. Latent (same as S5, except that there has been a lapse of 4 or more years since infection).

j. Ocular—

1. Iritis.
2. Keratitis.
3. Chorioretinitis.

Syphilis may occur congenitally—i. e., by the mother infecting the fetus through the placenta—and by various means of direct and indirect contact between individuals. By far the most common way of acquiring syphilis is through sexual intercourse with an infected individual who has genital lesions. Yet, infection on the genitals has taken place when no syphilitic lesions could be found in the partner. It may be possible that the semen and uterine discharges at times contain spirochetes. Occasionally, chancres known as extragenital are found on other portions of the body. A few of these come from sexual perversion but the majority occur on the mouth from kissing. It is possible for an infection to take place through an intermediate carrier of the organisms, such as a pipe, razor, towel, or drinking glass, but this is a rare circumstance. Infection from a toilet seat is often alleged by patients, but I doubt such an instance ever has been proved. Physicians, nurses, and midwives occasionally acquire chancres on the hands as the result of handling infected persons, and wet nurses have been infected by the children they suckled. In some backward regions, the custom of prechewing food for infants prevails, and syphilis has been transmitted in this manner, the chancre usually appearing on the infant's tonsils or neighboring areas of the mouth. Infection by blood transfusion takes place more frequently than it should. Indeed, transfusion syphilis threatens to replace the old vaccination syphilis and the chancre arising from the passage of a dirty eustachian catheter.

The commonest type of innocent infection is the venereal exposure of a wife by her husband or vice versa. Dudley Smith has reported a number of instances where children were infected by their parents. The usual

estimate is that more than 20 percent of all syphilis is acquired innocently, meaning *not* as the result of illicit sexual intercourse.

Even at present, we are still uncertain how long an infected person may transmit syphilis. The primary and secondary stage lesions swarm with spirochetes. They constitute the major phases of infectiousness. Mucocutaneous relapses are very contagious, and some inadequately treated cases undergo these relapses for a number of years. Usually an infected person represents no great danger 4 years or more after the date of his infection. The syphilitic who is least likely to be infectious is the one receiving regular and adequate treatment.

Pathologic Differences in Negro and White

While extragenital chancres are rare, squamous palmar syphilids unusual, and neurosyphilis less frequent in the Negro, certain other manifestations of syphilis are more characteristic of the Negro than of the white syphilitic. The frequency of annular lesions constitutes a dermatologic peculiarity of the Negro. Papular and follicular lesions are also more

Table 15.—*The race and sex prevalence of various syphilitic lesions (after Turner)*

Type of lesion [1]	Percentage of frequency in—			
	Whites		Negroes	
	Males 2,213 cases	Females 1,225 cases	Males 2,804 cases	Females 3,758 cases
Early syphilis: [2]				
Eye	3.5	1.9	9.5	4.9
Skeletal system	.4	.6	3.1	1.7
Nervous system	6.4	2.8	3.1	1.7
Late syphilis: [3]				
Skin and mucous membranes	7.8	11.6	9.0	8.3
Bones and joints	6.0	5.8	12.6	8.6
Cardiovascular syphilis:				
Aneurysm	1.2	.3	3.0	0.7
Aortic insufficiency	2.8	1.4	5.0	1.5
Aortitis and other forms	4.7	3.1	9.9	5.0
Neurosyphilis:				
Paresis	8.4	5.0	2.0	.3
Tabes	13.9	4.6	3.5	.8
All other types	17.0	12.6	10.4	5.9
Latent syphilis	40.3	55.9	41.5	66.4

[1] The prevalence of some lesions in which there are no striking race or sex differences is omitted.

[2] In this group, the percentages are expressed in terms of the total number of patients with early syphilis.

[3] In this and following groups, the percentages are expressed in terms of the total number of patients with late syphilis.

frequent. Late serpiginous syphilis is more common. Aortitis is much more common, as well as cardiovascular syphilis in general. Lymphadenitis in both early and late syphilis is much more frequent. There is disagreement over mouth lesions, although they are probably somewhat more frequent in the white race. Stricture of the rectum was formerly regarded as a syphilologic peculiarity of Negro females, but it is now believed that venereal lymphogranuloma is the usual cause. Iritis is more common in the Negro. Syphilis of the bones and joints is about twice as frequent. Condylomas are frequent in Negro women, and may be one reason for the prevalence of the disease in the race. Gumma of the testicle is more common in Negro than in white males. Mucous patches are much less frequent according to some evidence. Turner (*17*) reviewed the prevalence of lesions by race and sex in 10,000 consecutive syphilis cases at Johns Hopkins Hospital, the results of which are summarized in table 15.

The Chancre

About 93 or 94 percent of chancres among white persons are found on the genitals, while in Negroes the percentage is around 99. In some 30 years' experience with syphilis in the Negro, during which I have seen 561 patients with genital chancres and 2,342 with secondary lesions, I have seen only 15 with extragenital chancres despite a constant search for them. The 15 constitute only 0.53 percent of all primary and secondary lesions observed. During the same time extragenital chancres among white patients seen totaled 7 percent. The 15 extragenital lesions were distributed as follows: Lip 10, tonsil, 2, breast 1, finger 1, groin 1. The suggestion was made by Reasoner that the tissue of the Negro has a defense against initial syphilis infection with the single exception of the genitalia. Pusey, on the other hand, believes that the scarcity of extragenital infections may be due to "a lack of amatory preliminaries." Bearing on this point, many Negro physicians concede that theirs is not a "kissing race."

The clinical manifestations of any chancre in white or colored races have no essential difference, however (Figures 2 and 3, pages 84, 85). Induration may usually be noted at the edges, and if this induration be marked the lesion is called a Hunterian chancre. Some ulceration usually occurs in the center, so that the appearance is one of granuloma. Chancres may have a number of complications—there may be a mixture of chancroidal infection which causes a larger ulcerating mass. More rarely, they are phagedenic or spreading, probably implying a mixed infection of some type.

While most common, genital chancres are not always easy to find. They may be concealed, as in the case of the intraurethral chancre in the male and the common cervical chancre in the female.

When a chancre heals a small but plainly visible scar usually remains, a sign of considerable value in diagnoses made in later stages.

Multiple chancres occur not infrequently. They may develop all at the same time, or one or more may appear 2 or 3 weeks later.

The neighboring lymph nodes begin to swell within 2 weeks after the initial lesion has appeared. This is of particular value in diagnosing lesions of the mouth; the cervical nodes become very large and hard, and can easily be aspirated for the spirochete.

Since such common conditions as herpes or a slight trauma may be exactly simulated by the earliest syphilitic lesions, *Spirochaeta pallida* must be found to prove the diagnosis. They can be seen only by a microscopic examination with the dark-field technic. It is true that if the patient has treated the chancre with some antiseptic, the spirochete may not be found upon the first examination. In case the lymph nodes are enlarged, the node should be punctured and the material submitted for dark-field examination. If this is also negative, repeated examination should be made. Serologic examinations of the blood are usually negative during the first 2 weeks but with a sensitive test should be positive thereafter. If the dark-field examinations are negative and the first serologic examination also negative, the so-called "Wassermann follow-up" system should be employed, that is, one or two tests a week should be made for at least 6 weeks. If the tests are still negative and the patient has exhibited no other signs of syphilis, he may be discharged.

Several diseases may be mistaken for genital chancres—gonorrhea (for intraurethral chancre), chancroid, granuloma inguinale, venereal lymphogranuloma. Bacteriologic examination and the Frei test will assist in differentiating these conditions from syphilis. Scabies can be differentiated by the distribution of the cutaneous manifestations and the severe itching. Cancer can be told by the slow onset and the late development of lymph-node enlargement. Chancres of the lip are most apt to be confused with cancer but are of more rapid development, and the draining lymph nodes enlarge at a much earlier date (Figure 4, page 86). Cancer develops in older people and is almost invariably upon the lower lip. Laboratory tests will tell the difference; one should remember that cancer can develop in a subject with a positive Wassermann reaction, however. Chancre of the tonsil can and does simulate diphtheria, Vincent's angina, and lymphosarcoma. Results of dark-field examination of material taken from mouth and pharynx must be interpreted with extreme caution because of the occurrence of non pathogenic spirochetes which are very difficult to differentiate from *Spirochaetae pallidae*. If, however, the material has been obtained by gland puncture, there is no danger of confusion. Curiously enough, extra genital infections are usually confused with tuberculosis, which gives a totally different picture, or with a chronic bacterial or fungus infection.

Secondary Syphilis

Secondary syphilis is often thought of as the stage of the cutaneous rash. This is only partially true; the rash is one phase of a widespread infection which is a true septicemia.

In addition to the rash, enlargement of the cervical, inguinal, epitrochlear, and often the axillary lymph nodes may be found. In nearly half of the patients some enlargement of the spleen can be detected. Mucous patches may develop on the lips, tongue, buccal membranes, or on the pillars of the fauces but usually appear somewhat later than the rash. These patches are very contagious, and it is probable that most of the chancres about the mouth are due to kissing a person who has them. Transitory arthritic pains are very common and are generally believed to be due to actual invasion of the serous surfaces by the spirochete; the joints most frequently involved are the elbows and knees, but other large joints may be painful. Headaches are common; they are probably due to an involvement of the meninges. They are a sign which should be taken seriously. Alopecia is rather rare before the third month; it usually occurs in small spots not completely denuded of hair and most commonly found on the occiput. Fever is a fairly frequent accompaniment of pustular syphilis, especially if it is severe. As a rule, the temperature does not exceed 102° but it may make differentiation from smallpox difficult. Indigestion and even vomiting can be associated with acute secondaries. Some industrious person has shown that the flow of gastric juice is occasionally altered by syphilis. In the Negro, iritis is not uncommon. Anemia of the secondary type is common in women but not so marked in men. Transitory albuminuria is rare.

The skin manifestations of the secondary stage, generally known as early cutaneous syphilis, may be classified as follows:

Forms	*Varieties*	*Descriptive adjective*
Macular.	Roseolar.	Large, small.
	Annular.	
	Vitiligoid.	
Maculopapular.		Wheal-like, annular.
Papular.	Follicular.	Disseminate, annular.
	Raised.	Large, small, disseminate, annular, hypertrophic, confluent, squamous.
	Flat.	Large, small, disseminate, annular, moist, squamous.
Papulopustular.		
Pustular.	Accuminate.	
	Obtuse.	
	Ecthymoid.	Crusted, ulcerative.

The ordinary roseolar macular syphilis is the most common form in the white race but not in the Negro. It is true that a very faint macular eruption might not be noticed in a vary dark Negro because of the pigment, yet if such a patient is examined in a good light or under a blue lamp the eruption can often be distinguished. The macular lesions appear often in the light mulatto. Among 2,844 consecutive cases of early eruptive syphilis in the Negro, I saw 70 instances of macular syphilids and 130 instances of maculopapular eruptions (*23*). Perhaps the most common conditions

from which macular eruptions must be differentiated are measles, drug eruptions, and pityriasis rosea. Measles gives other definite symptoms including fever. Drug eruptions almost invariably itch intensely. Pityriasis rosea presents elongated oval patches which scale early and are parallel with the direction of the ribs.

Annular macular syphilids appear to be exceptionally rare in the Negro; not a case has been reported in my clinic in the past 20 years. They are scarce in the white race but are occasionally seen.

The vitiligoid eruption, or leukoderma, does not occur usually until at least a year after infection. White or light colored patches on the neck characterize it, and increased pigmentation in the surrounding area is infrequent. It is much more common in women than in men, and is probably due to a disturbance of the sympathetic nervous system associated with neurosyphilis. Comparatively few cases are seen. When it appears, a spinal puncture is absolutely essential. It should be remembered that vitiligo is not necessarily caused by syphilis.

Maculopapular lesions, being slightly raised, resemble the wheals of hives (Figure 5, page 87). These lesions, however, do not itch. Other signs of syphilis are generally present.

Papular lesions are so distinctive of syphilis in the Negro that an acute secondary eruption in the Negro may be expected to be papular. There is a slight tendency for the papular lesion to itch, a characteristic totally lacking in the white race.

The miliary or follicular eruption is not infrequent in the colored (Figure 6, page 88). These lesions may be widely disseminated or may be limited to the upper portion of the trunk. The individual papules may be slightly pointed or distinctly semiglobular, but they always arise around the hair follicles. They may group themselves in an annular eruption. They are simulated by no common disease.

Flat papules are frequent (Figure 7, page 89). They vary in size from $\frac{1}{16}$ of an inch to about 1 inch in diameter. Scales, often of silvery appearance, cover them. This type is at times disseminated over the entire face, body, and limbs, but is occasionally confined to a particular area. While flat papules are difficult to differentiate from the early lesions of psoriasis, it should be remembered that the dark-skinned Negro rarely suffers from this disease. Lichen planus may also constitute a difficulty in differentiation but the lesions of this disease are usually violaceous in color and not scaly; they itch intensely. Like all other papular lesions, the flat may become annular.

The raised lesions may be pointed, rounded, or semiglobular (Figure 8, page 90). They are widely disseminated, and the face is often affected. They vary in size from $\frac{1}{8}$ to $\frac{1}{2}$ of an inch or even more. A few central scales may or may not exist. They not infrequently show some increase in pigmentation. One fairly common variety, in which a few or many of the lesions may reach a diameter of more than $\frac{1}{2}$ inch, is the semiglobular

nodule. This type has not received the attention it deserves. It almost exactly simulates sarcomatosis. The smaller papular lesions can be confused with eczema, which is usually sharply localized and itches intensely. Another type is frambesiform—the lesions being berry-like in appearance and of a diameter from ½ to 1 inch. The lesions are practically identical with those of yaws. Their propensity for disappearing without treatment is amazing. They are much more frequent in the Negro than in the white.

Annular syphilis has been described by many (*24*, *25*, *26*, *27*, *28*, *29*) as the most characteristic syphilitic lesion of the Negro (Figure 9, page 91). In 2,844 cases of secondary syphilis (*23*), I found 478 instances of this type of lesion. The lesion is of two distinct types: First, lesions arising from the grouping of several papules; second, those arising from a single papule. Thus they may arise from large or small papules either discoid or lenticular, from grouped follicular lesions, and from papulosquamous lesions. Annular lesions are most frequent on the face, unusual on the limbs. Occasionally they are found on the mucous membranes of the mouth. They may be found in congenital as well as acquired syphilis, though they are less frequent in the former.

Condylomas, or moist papules, affect nearly every Negro woman with florid syphilis (Figure 10, page 92). The perineal lesions are both more numerous and larger than in white women. Curiously enough, it is unusual to find such lesions in the axillae or submammary folds. Negro men are likewise more prone to such papules than are white men.

Papulopustular and small pustular secondary syphilids are much more common in Negroes than in whites. Among my 2,844 cases, there were 141 of these, substantiating similar observations of other writers. Fever and general prostration may accompany these eruptions, giving the picture a strong resemblance to smallpox. In smallpox, however, fever is almost invariably present, and there is usually a history of chills or chilliness and often of severe backache. Then, too, pustular lesions on the palms and soles are much more frequent in smallpox than in syphilis. Generalized lymphadenopathy and lesions of the mucous membranes do not occur in smallpox.

Recurrent secondary eruptions may consist of any of the small papular types of the lesions already described, although the follicular type is rare. Recurrent secondaries tend to be grouped in rings.

The obtuse pustular syphilids are probably most common on the scalp but may occur on most any portion of the body. They are flat and vary in size from ¼ to ¾ of an inch. They are covered with a soft scab from beneath which pus oozes. The ecthymoid lesions are so similar that differentiation is almost impossible. It should be noted, however, that at times this latter type has a considerable depth. Often both obtuse pustular and ecthymoid lesions can be distinguished from the ordinary pyodermas only by finding other signs of syphilis.

It should be remembered that the blood tests are almost invariably strongly positive in the presence of a secondary syphilitic eruption.

Latent Syphilis

Latent means *hidden*. This describes the stage of syphilis where clinical symptoms have virtually disappeared but the disease actually may be "boring from within" in aorta, nervous system, bones, viscera, or other structures and causing damage which will not be manifest until later. The stage is classified as early latent and late latent. Early latency begins with the disappearance of the acute secondaries and, by definition, includes any latent period occurring within 4 years after the appearance of the chancre. Late latency is applied to all latent periods after the infection is 4 years old. The late latency may continue 40 or more years before an acute outbreak takes place. One should understand that it may be interrupted by the development of lesions in any portion of the body at any time. Again, the infection may never progress to late lesions, but actually remain static.

Moore (*30*) estimated that at any given moment at least one-third of all syphilis patients are in a latent stage. A 1937 study of the stage of syphilis on admission of 19,071 patients (*18*) in Chicago showed 10.6 percent early latent and 43.6 percent late latent, or a total of 54.2 percent. In a resurvey (*19*) in 1939, the latent cases totaled 66.6 percent of 18,481 cases. Keidel (*31*) believes that latent syphilis is much more prevalent in Negro females than in any other race-sex group, and Turner's study of 10,000 cases supports him (*17*). The percentage of latent cases among Negro females was 66.4 compared to 41.5 for Negro males and 55.9 for white females. This may be due to the tendency of pregnancy to ameliorate the course of the disease. It was once believed that a nonsyphilitic mother could bear an infected child and in this event she became permanently immune to syphilis (Colles' law). We now know that in this case the mother has latent syphilis suppressed by pregnancy. Another belief was that if a woman with secondary syphilis bore a healthy child it would be immune to syphilis (Profeta's law). But the serologic test usually indicates that the child has latent syphilis.

It is characteristic of the Negro patient to show a much more marked lymphadenopathy in latent syphilis than the white patient. The lymph nodes ordinarily affected are the epitrochlear and the cervical.

The only dependable pathologic evidence of a latent infection, however, is a positive reaction to a serologic test for syphilis.

Late Syphilis

All syphilis is classified as late 4 or more years after its onset. This is an arbitrary division from the pathologic, clinical, and epidemiologic standpoint because a contagious relapse with acute secondary symptoms of the skin or mucous membranes may occur after 4 years. Such mucocutaneous relapsing produces the same septicemia found in the secondary stage, and may occur at any time up to 10 years although it is most frequent within the first 4 years. Infectious relapses occur more frequently in males

of both white and Negro race than in the females. It may also be noted that late lesions of skin, bone, and eyes are much more apt to develop in the Negro than in the white. White patients are more liable to nervous system involvement; Negroes, to cardiovascular.

Late syphilis takes many forms, of which one or a half dozen may occur in the same individual. Lesions of the aorta are most common in Negroes, but involvements of the nervous system, periosteum, and skin are also frequent. Among the less common are joint lesions, cirrhosis of the liver, gumma of the lymph nodes, iritis, and iridocyclitis, ulceration of the throat with displacement of the uvula from scar tissue, and perforations of the soft palate. Gumma of the kidneys may occur, and syphilitic tumors and ulcerations of the stomach and of the large intestine have been reported. The suprarenal glands frequently show changes at autopsy although it is unusual to find clinical manifestations. The thyroid gland is affected rarely.

That aortitis very commonly results in either aneurysm or aortic insufficiency is of particular interest. The nervous manifestations may be meningitis, vascular changes particularly in the cerebral vessels arising from the circle of Willis, solitary gummas, acute myelitis, optic atrophy, tabes dorsalis, and paresis. Hundred of cases of blindness, insanity, and Charcot's joints arise annually from syphilis.

While malignant, destructive lesions identical with late cutaneous syphilis may appear a few weeks after the initial skin manifestations, late cutaneous lesions ordinarily do not appear until at least 2 years have elapsed. They may be classified as follows:

Forms	*Varieties*	*Descriptive adjectives*
Nodular.	Agminate.	Confluent, squamous, cicatricial.
	Circinate.	Squamous, crustaceous, ulcerative.
	Serpiginous.	Crustaceous, ulcerative, cicatricial.
Squamous.	Diffuse.	
	Circinate.	
Gummatous.	Diffuse.	Verrucous, crustaceous, rupial, ulcerative.
	Tuberous.	Ulcerative, cicatricial.

The late lesions are usually more localized than are the early ones. They may occur in any organ of the body as well as in the skin. They are likely to break down within 6 months of their first appearance. There are occasional exceptions, and squamous lesions on the palms and soles form an almost total exception.

Nodular syphilis is the "tubercular syphilis" described in the texts of earlier writers. Many students and physicians have acquired the mistaken idea that tubercular syphilis is a combination of tuberculosis and syphilis, and hence it seems best to liquidate the term.

Agminate nodular lesions are rounded or conical papules or nodules. They may be discrete upon first appearance, but they usually coalesce to form a patch or raised nodule. They commonly occur on the face and limbs but frequently develop on the trunk as well. The size varies from

⅛ to nearly ½ inch in diameter, but may increase to some 2 inches when confluent. They become covered with heavy scales and are then described as squamous. The lesion may resolve spontaneously with or without scar formation; the scars are known as cicatricial lesions.

The circinate and serpiginous types need not be separated (Figure 11, page 93). Both consist primarily of agminate lesions. They extend peripherally or by the formation of new lesions so as to form round or spreading patches which may attain a diameter of from 4 to 12 inches. The limbs and body are the most common sites. The patches usually clear up at the center with or without scar tissue formation. Ulceration may or may not take place at the edge. The course is always extremely slow, and the lesions are usually painless. The serpiginous lesions are much more common in the Negro than in the white and are sometimes spectacular.

The squamous lesions occur primarily on the palms and soles. They are doubtless primarily nodular but the thickness of the skin makes them appear scaly or plate-like. At first a number of thickened patches appear, usually in the deep lines; then some scaling and cracking occurs, and the patches extend so they become confluent. The edge is well-defined and may show ulceration. The color is a deep red overlaid by whitish scales. They develop very slowly and are resistant to treatment. It is difficult to diagnose them from eczema or from ringworm occurring on the palms and soles. It is surprising that these late squamous lesions are infrequent in the Negro since the florid secondary lesions of the palms and soles are relatively common.

The tuberous gummas, especially common to the face, are of a more superficial development than the typical gumma. They develop in patches of an inch or more in diameter. In the Negro the follicular openings are frequently very marked. These lesions may persist for years but usually break down within 6 months.

The diffuse gummatous syphilid is comparable to the diffuse, or cirrhotic, changes occurring in the tongue and viscera. An area of one foot in diameter may be involved in the process, which is primarily situated in the corium. At first the skin is a livid red color with deep infiltration, so that it feels stony hard to the touch. Portions usually break down forming typical ulcers (Figure 12, page 94).

The basic characteristics of late syphilis have been summarized (*32*) in 10 points, as follows:

1. Solitary or few lesions.
2. Asymmetry.
3. Induration; deep palpable infiltration.
4. Indolence; low-grade inflammatory process.
5. Arciform polycyclic borders forming segments of circles, both in individual lesions and in configuration groups.
6. Sharp margination; "punched out" ulcers.
7. Tissue destruction and replacement with or without ulceration.
8. Central or one-sided healing with peripheral extension.

9. Superficial, atrophic, noncontractile scar with arciform configuration of original lesion.
10. Persistent peripheral hyperpigmentation.

Common skin conditions in the Negro which may be confused with late syphilis are tuberculosis, leprosy, pyoderma, skin cancer, varicose ulcers, erythema nodosum, lymphoblastoma, sarcoma, furunculosis, carbuncle, sarcoid, acne rosacea, and traumatic ulcers.

Tuberculosis usually develops much more slowly than syphilis and is prone to affect younger persons.

Leprosy develops more slowly; there is anesthesia in one type; the lepra bacillus can be found; thickened nerves can be demonstrated.

Pyoderma usually shows multiple lesions that generally are more superficial than those of syphilis and is more common in young persons.

Skin cancer develops slowly, is more common in the aged, and usually has a hard ring of induration.

Varicose ulcers nearly always occur low down on the legs; generally varicose veins are present. Very frequently some eczema surrounds these ulcers.

Erythema nodosum appears suddenly with more or less painful nodules on the legs and occasionally on the arms. It should always be borne in mind that there is a syphilitic form of this disorder.

Lymphoblastoma shows many clinical forms. The lesions are usually multiple and symmetrical; there may be intense itching, and the blood often shows characteristic changes.

Both sarcoma and sarcoid, which may be a form of tuberculosis, may be difficult to differentiate from syphilis, but neither gives a positive serologic reaction.

Furunculosis is usually superficial, painful, and starts in around the hair follicles. The lesions last but a short time.

Carbuncles come on very abruptly and have multiple areas of discharge.

Acne rosacea is extremely rare in the Negro. As a rule there are no destructive lesions.

Traumatic ulcers come on abruptly, and there should be a history of injury.

It is sometimes necessary to resort to the therapeutic test in order to differentiate these conditions from syphilis.

Syphilis of the Nose and Mouth

Chancres and condylomas of the nostrils are rare. By far the most common of the nose lesions are those occurring in late acquired or congenital syphilis and involving either the bone or the cartilage of the septum. In the latter case, perforation of the septum usually occurs, but perforation can be caused by other diseases.

Syphilitic lesions within the mouth are relatively common. Initial lesions may occur on the lips, tongue, or tonsils as already discussed. Both secondary and late lesions within the mouth are common in both races, but are probably somewhat more common in the white race. Mucous patches are most frequent, usually appearing on the lips but also occurring on the edges of the tongue and its dorsum as well as on the pillars of the fauces, buccal mucosa, and roof of the mouth. They vary in size from ¼ to ¾ of an inch, the larger ones probably being due to the confluence of several patches. The lesions may be covered by a dirty gray, adherent membrane. They swarm with spirochetes. They may be tender and are occasionally painful. If the mucous patches are located in the pharynx the patient usually complains of sore throat. These lesions must be distinguguished from erythema multiforme, Vincent's angina, and aphthous stomatitis (canker sores). This should not be done with the dark-field microscope because even a normal mouth teems with spirochetes of other varieties, some of which strikingly resemble *Spirochaetae pallidae*. A blood test is more certain. Rarely syphilitic papules or even annular lesions may occur on the lips, dorsal surface of the tongue, or roof of the mouth; apparently this always takes place as part of a generalized eruption so the diagnosis is not as difficult as might be supposed.

Leukoplakia may be a late development of syphilis and is usually found upon the dorsal surface of the tongue, although it may occur on the buccal mucosa. This condition is probably due to a diffuse gummatous deposit in the superficial layers of the tongue, although the entire musculature may be affected. Leukoplakia is extremely rare in the Negro race. Tobacco often has been blamed as a concomitant cause, but this is somewhat doubtful. The lesions first appear as closely adherent white patches which gradually spread until the entire dorsum is covered, then producing a number of cracks and fissures which are usually intensely painful. An unfortunate complication is the fairly frequent development of cancer in these lesions.

The treatment of leukoplakia is notoriously unsatisfactory. Out of some 40 cases that I have seen, there was one instance in which the condition was helped by antisyphilitic treatment. Both Roentgen rays and radium are notorious failures, and surgery has but little to offer. A patient suffering from this complication should be treated for syphilis; his mouth should not be irritated by tobacco, rough teeth, faulty dentures, or excessively hot or cold foods or drinks, or by condiments.

The so-called "cobblestone tongue" usually develops somewhat earlier than leukoplakia. This also is due to a diffuse syphilitic process through the musculature of the tongue, and is accurately described by the name. The surface of the tongue is deeply indented by transverse and longitudinal fissures which vary in depth from 1/16 to nearly ¼ inch. The fissures run approximately ½ inch apart. Antisyphilitic treatment may markedly benefit this condition.

Smooth atrophy of the base of the tongue is not infrequent in late syphilis. Unfortunately a search is seldom made for it. The mucosa is smooth, atrophied, and distinctly hard to the touch.

A solitary gumma may affect the tongue. This occurs deep within the muscles and may grow to be almost as large as a hen's egg. It is frequently mistaken for sarcoma. Any large lump within the tongue is an absolute indication for a serologic examination because the gumma can be readily cured by proper medication.

Gummatous ulceration of either the roof of the mouth or of the posterior portion of the pharynx and occasionally of the tonsils may occur. Such a process in the roof of the mouth leads to a perforation of either the hard or soft palate. A perforated palate leads to suspicion of syphilis. If these cases are recognized at the onset, they are usually healed under anti-syphilitic treatment but once a perforation has persisted for some time it cannot be closed by medication. Syphilitic ulcerative processes about the pharynx or tonsils often produce a considerable amount of distortion caused by contraction of scar tissue. They may reach serious proportions before they are recognized. Occasionally they are mistaken for cancer, but one or two injections of arsphenamine should settle the question beyond doubt.

Syphilis of the Respiratory and Digestive Tracts

Syphilis of the larynx is not uncommon. It is well known that a marked hoarseness may accompany either the early or late stage of syphilis. This may be due to a simple inflammation, to actual papules on the larynx, to destructive processes either in the mucous surfaces of the larynx or in the surrounding cartilages, or to involvement of the recurrent laryngeal nerve by aneurysm. Laryngoscopic examination will often reveal the nature of the difficulty. Other conditions cause similar trouble in diagnosis; among them are tuberculosis, leprosy, cancer, and a simple chronic inflammation. A serologic examination should be made in all cases of hoarseness persisting more than 10 days.

Syphilis of the trachea is a rarity characterized by marked dyspnea. Connor (*33*) has described the condition admirably.

Syphilis of the lungs is likewise unusual. Many authorities claim that the only type is the pneumonia alba of the stillborn. This has not been wholly true in my experience. I have seen three cases in post mortem examination of Negroes. In these, the lesion was diffuse resulting in solidification of the entire lower lobe or of the two lower lobes. Such patients, of course, present the symptoms of a chronic respiratory distress and sometimes show considerable elevation of temperature. Care must be taken in accepting the roentgen-ray diagnosis of this condition because it may be extremely difficult to differentiate from tuberculosis of the lower lobe.

The parotid glands are sometimes invaded. When this occurs in the late stages, the glands are much enlarged, nodular, painful, and the salivary secretion is usually markedly reduced. This condition may resemble mixed tumors or even malignant tumors of the parotid, although their

development is likely to be more rapid. The patient does well under antisyphilitic treatment.

The rare syphilis of the esophagus has been fully described by Wile (*34*). The symptoms are those of an obstruction and must be differentiated from carcinoma.

Syphilis of the stomach is rare but does occur; about one percent of the tumors of this organ are probably syphilitic. The characteristic "water bottle stomach" may be malignant but can also be syphilitic in a fairly high percentage of the cases. Every patient suspected of having a malignancy of the stomach should have a serologic examination, for occasionally this procedure may save a life.

Syphilis of the small and large intestines is so rare that it need not be discussed.

Syphilis of the rectum, according to tradition, is particularly common in the Negro female. There is no doubt that a stenosis at this point is relatively frequent in the colored woman. Many, if not most, occurrences of this kind, however, can be attributed to venereal lymphogranuloma. The use of both Frei and serologic tests often makes differential diagnosis possible, although the Frei antigen is not always active. Also, both conditions may occur in the same patient. The question of the relative frequency of rectal stenosis caused by syphilis and by venereal lymphogranuloma is still unsettled, although the preponderance of recent evidence seems to favor the latter disease as the cause of the vast majority of nonmalignant rectal strictures.

Syphilis of the liver is important and not infrequent. An involvement of the capsule will produce the characteristic "hob-nail" liver, although diffuse carcinomatosis or even leukemia may produce the same picture. When the liver itself is involved, the hypertrophic type is the more common. This is often associated with ascites. A considerable destruction of the liver tissue takes place and naturally interferes with the function so that the patient suffers from chronic digestive disturbances. There may be a marked rise in temperature. Hepatic syphilis may resemble a long list of diseases including:

Laennec's cirrhosis.
Carcinoma of liver (primary or secondary).
Tuberculous peritonitis.
Myocardial failure with hepatomegaly and ascites.
Cholecystitis.
Echinococcus cyst.
Amyloid disease.
Cyst of kidney.
Hodgkin's disease.
Hepatic amebic abscess.
Hepatic abscess.
Chronic splenic anemia (Banti's syndrome).
Retroperitoneal tumor.
Pancreatic cyst.
"Catarrhal jaundice."
Gastric or duodenal ulcer.
Malaria.
Leukemia.
Disseminated carcinoma of the peritoneum.
Abdominal aneurysm.

Syphilis of the heart and blood vessels is one of the most destructive forms of the disease, both as a crippler and a killer. Many authors have reported on its greater frequency in the Negro race, and a review of their work indicates that the cardiovascular syphilis rate among Negroes is at least twice as high as that among whites, with the frequency ratio even greater in cases of aneurysm and aortic insufficiency (*17*, *28*, *32*, *35*, *36*, *37*, *38*, *39*, *40*, *41*, *42*, *43*, *44*, *45*, *46*). Following is a classification of the more important types of cardiovascular syphilis:

Heart	*Aorta*	*Peripheral vessels*
Myocarditis.	Aortitis.	
Aortic insufficiency.	Aneurysm.	
Pulmonic valve insufficiency.		
Heart block.		
Aneurysm of heart.		
Coronary sclerosis.		

Cardiovascular syphilis is distinctly rare in congenital syphilis, no matter what the race or sex.

Myocarditis due to syphilis is practically impossible to distinguish from myocarditis due to numerous other causes. The electrocardiographic tracings are identical in the contrasting conditions. It has been claimed that spirochetes could be distinguished in the heart muscle, and that the disease was primarily due to a direct invasion of the heart muscle fibrils by the organism; in other words, it was not primarily a disease spreading along the course of the blood vessels. This view, however, apparently has been disproved. In any event, there are two types of syphilitic myocarditis, the acute type occurring simultaneously with the secondary stage and the chronic type developing at some period late in the disease.

The acute type, a rarity, can be distinguished by time of occurrence, rapid pulse, weakness of heart sounds, shortness of breath, cyanosis, and general prostration. This type demands arsphenamine therapy at the onset. If the treatment is started sufficiently early, the results are excellent.

The chronic type has precisely the same symptomatology as myocarditis in general. Again there is a rapid and irregular pulse, some shortness of breath, cyanosis at times, and later broken compensation. The treatment of this type of syphilitic myocarditis is eminently unsatisfactory. If arsphenamine is used, the dosage should be low and should be preceded by 3 or 4 months of bismuth therapy. In general, bismuth injections probably constitute a safer form of therapy for the general practitioner. Naturally, the heart must be treated along the lines of general management, i. e., rest, suitable food and care, with digitalis or other cardiac stimulants.

Aortic insufficiency is the commonest valvular lesion found in the Negro. It is usually due to syphilis in contradistinction to mitral lesions which are seldom caused by this disease. The symptoms of syphilitic aortic insufficiency are those of aortic insufficiency from any other cause. Attacks of

broken compensation are more frequent in the Negro, doubtless because of his heavy work. Advanced cases of this affliction can often be told by inspection alone. There is a throbbing of the carotid arteries, a precordial heave, and, upon slight pressure, an obvious pulse beneath the finger nails. The point of maximum impulse of the heart is downward and outward. Upon palpation, a distinct heave can be felt over the heart. Also there is a distinct water-hammer, or Corrigan pulse. Upon percussion, there is an increase of cardiac dulness. Auscultation reveals a distinct diminuendo diastolic murmur which is widely transmitted. In early cases, this murmur, along the left side of the sternum, may be the only physical sign. There may be a Flint murmur at the apex.

Moore (*47*) and his associates have shown that life expectancy in this condition can be greatly increased by thorough and efficient treatment, and, although contrary views are held by many experienced internists, my own experience corroborates the finding that treatment is of benefit. Naturally, treatment should not be pushed during the period of broken compensation. Treatment during this time is essentially the same as for broken compensation in general.

Syphilitic disease of the pulmonary valves is uncommon, although cases have been reported. Both the symptoms and physical signs are largely the same as in the nonsyphilitic disease of the same type. Treatment is also similar, with the addition of antisyphilitic therapy.

Heart block, or Stokes-Adams disease, may be due to a gumma in the bundle of His. This is decidedly rare.

Syphilis may produce aneurysm of the heart wall. It has been shown that there is no racial difference in the incidence of gumma of the heart (*40*).

Syphilitic aortitis sometimes encroaches upon the mouths of the coronary arteries and produces the signs and symptoms characteristic of coronary occlusion.

Aortitis is not invariably syphilitic, but syphilis is the cause in 97 or 98 percent of all cases. It is often stated that over 80 percent of all syphilitic patients examined post mortem show some evidence of this condition. The criteria given by the Cooperative Clinical Group of the United States Public Health Service follow:

1. Teleroentgenographic (anteroposterior and left anterior oblique positions) and fluoroscopic evidence of aortic dilatation, especially if localized to the ascending aorta.
2. Increased retromanubrial dullness.
3. A history of circulatory embarrassment, especially exertional dyspnea, with or without progressive cardiac failure.
4. A tympanitic, tambour, bell-like quality to the second aortic sound, with or without marked accentuation.
5. A rough systolic aortic murmur, usually transmitted upward, downward, or both.

6. Substernal, less frequently precordial, dull, aching pain, usually without radiation or relation to exercise.

7. Paroxysmal dyspnea, not exertional and usually nocturnal.

Therapeutic hope in aortitis lies in the recognition of the lesion before the development of aortic regurgitation or aneurysm. While uncomplicated aortitis is often clinically unrecognizable, it may, nevertheless, be diagnosed directly in a considerable portion of the cases. In a patient known to have syphilis, whether on the basis of serologic tests or history of infection, the presence of any three of the above-mentioned criteria makes almost certain the diagnosis of uncomplicated aortitis; the presence of any two makes the diagnosis likely, provided mitral disease is absent.

Aortitis or syphilitic heart disease may resemble:

Rheumatic heart disease.	Angina pectoris.
Arteriosclerosis.	Lymphosarcoma.
Essential hypertension.	Dissecting aneurysm.

The only safe procedure is to suspect syphilis in all instances and to check the suspicion by repeated serologic tests.

Aneurysm was associated with syphilis by several early writers, but only within the past 50 years has the disease been recognized as the cause of most cases of aneurysm. Probably a few cases of aneurysm of the aorta are due to other causes, notably arteriosclerosis.

The ascending portion of the aorta is the most frequent site, but any part of the thoracic aorta and even the abdominal aorta are occasionally involved. Other less frequent sites are the subclavian, the carotid, the femoral iliac, the popliteal, the innominate, and the axillary arteries, but in some of these locations syphilis is by no means the only cause. Thoracic aneurysms may be diffuse or they may be sacculated and circumscribed.

The symptoms are pain in the chest, intercostal neuralgia, oppression, difficulty in swallowing, a chronic cough, and hoarseness. The physical signs are localized pulsation, localized bulging of the chest wall, a thrill and diastolic shock, and a tracheal tug. However, the diagnosis can be made by roentgenologists with considerable certainty, although a soft mediastinal tumor may be difficult to differentiate.

Peripheral arteritis of syphilitic origin may take one of two courses: thrombosis or aneurysm. The lesions are practically always unilateral. We no longer hear Raynaud's disease, Buerger's disease, and the like attributed to syphilis.

Neurosyphilis

The general belief is that neurosyphilis is more common in the white than in the Negro race. Varying conclusions have been reached on the comparative frequency of syphilis of the central nervous system (*28*, *48*, *49*, *50*, *51*, *52*, *53*, *54*). A Cooperative Clinical Group study (*55*) of 5,293 syphilis patients who had spinal fluid examinations while under treatment

for periods of two or more years showed white males with symptomatic neurosyphilis outnumbering the Negro males in percentage frequency 5 to 3 and white females surpassing Negro females 3 to 1. Division of the neurosyphilitics by stage of syphilis upon beginning treatment showed a similar higher prevalence in the whites, although the ratios were not so high (see table 16).

In routine spinal fluid examinations of patients with secondary syphilis approximately 25 percent of positive reactions may be expected. In late syphilis, the figure varies, but the untreated cases approximate 23 or 24 percent while treated cases range anywhere from 4 to 20 percent depending on the thoroughness of treatment.

TABLE 16.—*Percentage incidence of neurosyphilis amoung 5,293 cases of syphilis that had spinal fluid examinations during treatment and observation periods of 2 years or more*

Classification	White		Negro	
	Males	Females	Males	Females
Total cases	2, 935	1, 316	472	570
	Percent	*Percent*	*Percent*	*Percent*
	14. 4	15. 0	9. 1	8. 6
Asymptomatic neurosyphilis	50. 9	31. 5	30. 7	10. 2
Symptomatic neurosyphilis	34. 7	53. 5	60. 2	81. 2
Negative				
Early syphilis	642	270	171	170
	Percent	*Percent*	*Percent*	*Percent*
Asymptomatic neurosyphilis	23. 4	25. 6	10. 5	11. 2
Symptomatic neurosyphilis	13. 9	10. 7	11. 1	5. 9
Negative	62. 8	63. 7	78. 4	82. 9
Late syphilis	2, 293	1, 046	301	400
	Percent	*Percent*	*Percent*	*Percent*
Asymptomatic neurosyphilis	11. 9	12. 2	8. 3	7. 5
Symptomatic neurosyphilis	61. 3	36. 9	41. 9	12. 0
Negative	26. 8	50. 9	49. 8	80. 5

Invasion of the central nervous system almost invariably takes place at the time of the widespread dissemination of spirochetes in the blood stream, that is, about the time of the secondary lesions. Neurosyphilis has developed later in many a patient whose treatment was begun within a week after the appearance of a chancre. It is possible that in 3 or 4 percent of neurosyphilis, infection of the central nervous system may take place during a later outburst of septicemia. The following classification is generally used for neurosyphilis:

1. Parenchymatous neurosyphilis—
    a. Tabes dorsalis—with or without optic atrophy.
    b. Paresis.
2. Meningeal neurosyphilis—
    a. Early.
    b. Late.
3. Meningovascular neurosyphilis—including paralysis of the oculomotor and other cranial nerves due to central involvement.
4. Neurorecurrence.
5. Solitary gumma.
6. Myelitis.
7. Optic atrophy.
8. Syphilophobia.

Both clinical and laboratory procedures are used in establishing a diagnosis of neurosyphilis.

The clinical examination should include:

1. Eye muscles—simple tests to determine whether there is paralysis or whether they tire quickly. It should always be remembered that there are many causes other than syphilis of eye-muscle fatigue.

2. Ophthalmoscopic—essential for a suspected chorioretinitis, optic neuritis, or atophy. There is considerable question whether this examination should always be made by an ophthalmologist or whether the good clinical syphilologist should train himself to do this work.

3. Pupils, irregular, unequal—suggestive but not necessarily due to syphilis.

Small, fixed to light—extremely suggestive, especially as a sign of advanced tabes.

Argyll Robertson pupils (small, irregular, unequal, and react to accommodation but not to light)—extremely suggestive of tabes.

4. The following reflexes should always be tested: Biceps, triceps, abdominal, patellar, and Achilles.[1] With the exception of the abdominal these are best tested with a small rubber reflex hammer. Reflexes should be tested for asymmetry, absence, and increase.

5. Romberg sign—Test by having patient stand with feet together and eyes closed. Be ready to catch the patient if he falls.

6. A search should be made for tremors of the extended tongue and of the extended and spread fingers.

7. Coordination may be tested by having a patient close his eyes and attempt to touch the end of his nose with the forefinger. The arm

[1] The Achilles reflex deserves to be better known for it is just as reliable as the patellar reflex and in many patients it is much easier to elicit. The patient should stand with one knee resting upon a chair so that the lower leg is horizontal. A gentle tap on the Achilles tendon, not done through a high shoe, should elicit a satisfactory response.

should first be held out horizontally and the movement should be very slow. Walking down stairs is also an aid. Also, speech coordination should be tested. Look for slurring of consonants, hesitancy, and confusion.

8. The heat and cold senses should be tested using ordinary test tubes filled with ice water and hot water. Areas of hypoesthesia or hyperesthesia should be investigated.

9. Psychiatric examination. Look for euphoria, delusions of grandeur, defects of memory and reasoning, emotional instability.

The laboratory examinations include tests of the blood serum and examination of the spinal fluid. It should always be remembered that in competent hands the latter is often a deciding diagnostic factor. It is not unusual, in many conditions, to find that the blood will be negative and the spinal fluid will be positive.

The spinal fluid may be obtained by spinal puncture or by cisternal puncture. The latter is probably more comfortable for the patient, but is not entirely free from elements of danger. I have seen at least three patients who died as a result of the needle puncturing a misplaced blood vessel. Spinal puncture is done in the routine way. The resulting headaches are very much lessened by the use of a relatively small gauge needle. The strength of the needle should be tested before using it; there have been a number of instances where the needle has broken off in the patient. For private patients it is probably preferable to have the patient enter the hospital for 48 to 60 hours. In dispensary work this is not always practicable, and as a substitute a number of beds should be provided in which patients may rest for some 8 hours following the tapping.

Four tests should be done on the spinal fluid; first, a cell count; second, a test for increased globulin; third, a serologic test; fourth, either a gold chloride or mastic test.

The cell count is done in the usual way. At the present time there is still some slight disagreement as to what the upper limit of cells should be in normal fluid. Certainly a count of more than 10 cells should be considered pathologic. An increased number of cells may be found in any inflammatory condition of the meninges.

The globulin may be estimated by the use of Pandy's fluid. This will also be increased in any inflammatory condition.

Either a modification of the Wassermann reaction or one of a number of flocculation tests may be used. It is rather disturbing to find that serologists will by no means always report uniform results in spinal fluid drawn from the same patient. This point has been emphasized in the report of the Committee for the Evaluation of Serodiagnostic Tests for Syphilis (*56*).

The gold chloride test has been replaced in some quarters by the mastic [2]

[2] The mastic test is much simpler than the gold chloride test and yields approximately the same information. It is well discussed in Harry Eagle's book, "Laboratory Diagnosis of Syphilis," p. 258.

test for the reason that the preparation of the solution is very much simpler and the opportunities for error considerably less. The test simply shows the relationship of globulin to the total protein content of the spinal fluid. Two types of reaction are given by the test. There may be a so-called "syphilitic curve," or there may be a paretic curve. The test is done with 9 or 11 tubes. In the syphilitic curve the greatest change takes place in the middle tubes in the series so that the reading will run 00135553100. In the paretic curve, on the other hand, the greatest change takes place in the first tubes so that the reading will be 5554310000. This latter type of curve by no means always indicates that the patient has paresis or is doomed to paresis. It should be remembered that a positive test can also be given by multiple sclerosis.

Differential diagnosis of neurosyphilis will be given separately under the various types of the disease.

Treatment of neurosyphilis differs from the treatment of syphilis lacking this complication. Practically all syphilologists are agreed that arsphenamine should be used intravenously rather than neoarsphenamine. The courses should comprise 10 to 12 injections at weekly intervals rather than 6 to 8 injections. Arsphenamine given intravenously will often work very well in all types of syphilis of the central nervous system, with the exception of general paralysis and some cases of tabes. The way to decide whether or not intravenous injections will be a benefit is to examine the spinal fluid, then give a course of 12 intravenous injections at weekly intervals, and then examine the fluid again. If considerable improvement has taken place in the fluid, as well as clinical improvement, another course of intravenous treatment may be given after some 4 weeks of bismuth injections.

A drug that is considerably used in all types of resistant neurosyphilis is tryparsamide. This drug is a clear white powder which is readily soluble in distilled water, and may be given in weekly doses of from 2 to 3 grams. A serious disadvantage of this drug is that it may cause blindness. Fortunately there are usually warning symptoms before this occurs. The patients are apt to complain of flashes of light before the eyes, and a surer method is to test the field of vision with a perimeter. Contraction of the visual fields indicates damage to the optic nerve. Fortunately if the drug is stopped the toxic process does not progress.

The most popular method of treatment of resistant neurosyphilis and particularly of paresis is by means of the well-known inoculation with malaria. The newest method, which has a considerable vogue in certain quarters, is the so-called "heat therapy" which is usually given in a special cabinet heated by electricity. Both of these methods will be described in the section dealing with therapy.

Intensive intravenous medication with old arsphenamine improves many cases of tabes dorsalis. Some cases are intractable to this form of therapy but are definitely cured by tryparsamide, and still others by either malaria or heat therapy.

Syphilophobia, of course, is not syphilitic but is included in this classification for convenience.

Tabes dorsalis, or locomotor ataxia, is due to an involvement of the deep sensory tracks in the spinal cord. The first symptoms may be some difficulty with vision or trouble with walking, especially at night. Distinct pains around the waist—the so-called "girdle pains"—are the first symptoms at times, and are occasionally mistaken for appendicitis. In other instances bladder disturbances, due to trabeculation, are first noted.

Later symptoms are blindness due to optic atrophy, Charcot's joints, difficulty in walking, sharp lancinating pains in the body and legs (the so-called "lightning pains"), loss of libido, sphincter disturbances, and perforating ulcer of the foot. Physical signs include the Argyll Robertson pupil, small fixed pupils, loss of knee and tendo achillis reflexes, and trabeculation of the bladder. The blood has been found to have a positive reaction in more than 60 percent of untreated tabetics, and the spinal fluid, in about 90 percent (*57*).

The differential diagnosis must be made from lesions of peripheral sensory nerves, tumors or chronic sclerosis of posterior columns, multiple sclerosis, subacute combined sclerosis of pernicious anemia, vestibular ataxia, brain tumor (optic atrophy), Leber's disease (optic atrophy), retrobulbar arthritis (Charcot's joint), syringomyelia (Charcot's joint), diabetic pseudotabes, infected callus of soles (malum perforans), and degeneration of the cerebellum.

Parcsis, or general paralysis of the insane, begins from 5 to 20 years after infection. Pathologic degeneration occurs in the cerebral cortex, and even involves the cortical nerve cells. There is some involvement of the meninges dipping down in the convolutions.

The first symptoms of paresis are usually psychic; the patient's memory and perception fail in varying degrees. The development of grandiose ideas is frequently the most noticeable feature. The delusion of grandeur commonly involves riches. The patient may disregard the conventions, be dirty in dress or in speech, and be indifferent to the feelings of others. He is prone to get into financial difficulties. There are often speech defects, particularly slurring, which may be tested by such stock sentences as "round the rugged rock the ragged rascal ran."

The blood is strongly positive in all but a small percentage, and the spinal fluid is almost invariably positive.

The gold chloride or mastic tests generally give a typical paretic curve. Patients presenting signs of both paresis and tabes should be diagnosed as having taboparesis.

The differential diagnosis must be made from neurasthenia, psychoneurosis, hysteria, simple depression, manic depressive insanity, schizophrenia, brain tumor (frontal lobe), cerebral arteriosclerosis, chronic alcoholism, epidemic encephalitis, lead encephalopathy, uremia, and epilepsy.

The treatment is not nearly as hopeless as it formerly was; there was a day when all of these patients were doomed to death, usually within a

space of 2 years. At the present time some 60 percent can be restored to a useful life. It was once a question whether the patients were really cured or undergoing a lengthy remission; but so many of them have remained well for 10 or more years that now there seems to be every reason for believing them cured.

Treatment should consist of malarial therapy (which will be discussed in part IV) followed by 2- or 3-gram doses of tryparsamide at weekly intervals. At one time there was a mortality of nearly 10 percent from the malaria, but at present a better selection of patients, particularly with regard to their vascular apparatus, has reduced this mortality.

Early syphilitic meningitis is usually indicated by more or less severe headache occurring about the time of the secondary symptoms' appearance. It was formerly thought that these headaches were due to toxemia, but it is now known that there is actual involvement of the cerebrospinal fluid. If the headache does not disappear after intravenous injections, it is well to do a spinal puncture early to determine whether or not the fluid shows changes of the preparetic type. If this should be the case, treatment must be pushed harder with old arsphenamine in courses of 12 injections each. The alternating courses of bismuth should be very short, not over 4 to 6 injections. Ordinarily no physical signs are given by this type of neurosyphilis.

In some cases of early syphilitic meningitis there are, in addition to headache, slight increases in the reflexes, possibly some changes in the pupillary reactions, and a general sense of malaise. This type can usually be controlled by trivalent arsenicals and bismuth although either tryparsamide or malaria may be necessary.

Mild meningeal neurosyphilis, occurring later, has a wide range of symptoms and physical signs depending upon the localization of the process. Patients are frequently regarded as neurotic or as suffering from "a nervous breakdown." Headache, inability to concentrate, nervousness, loss of weight, slight difficulties with vision, and possibly a change in disposition are common symptoms. Inequality and defects in the reaction of pupils and reflexes may be found. Areas of hyperesthesia are not uncommon. There is a moderate increase in both the cell count and the globulin content. The spinal fluid gives a positive serologic reaction, and the gold chloride curve is in the syphilitic zone. If intravenous arsphenamine therapy does not effect speedy changes either tryparsamide or malaria should be tried.

Severe meningeal neurosyphilis is similar but more severe and in its acute stage is often indistinguishable clinically from acute meningitis due to other causes. Optic atrophy is not uncommon and deafness may result. Other changes are ptosis or an internal squint. Tremor of either the extended tongue or of fingers is common. The blood serum reaction is practically always strongly positive, and in the spinal fluid, cell count and globulin are markedly increased. Treatment is the same.

Differential diagnosis, which can be carried on only in the laboratory, must be made from the following list of infections: Tuberculous meningitis, brain tumor, brain abscess, benign lymphocytic meningitis, peripheral neuritis, subacute combined sclerosis (pernicious anemia), acute or chronic anterior poliomyelitis, disseminated sclerosis, amyotrophic lateral sclerosis, syringomyelia, epidemic encephalitis, Bell's palsy, migraine, cord tumor, postdiphtheritic paralysis, chronic alcoholism, cerebral vascular accident, paralysis agitans, cerebral arteriosclerosis, and epilepsy.

Meningovascular neurosyphilis may occur from 2 to 40 years after infection, and thus involve either young or old. The vascular complications usually arise in the smaller arteries which emanate from the circle of Willis at the base of the brain. Two types of lesions may be found in these vessels, minute aneurysms or thrombotic processes.

The symptoms, depending upon the localization of these changes, may be sensory or motor, the latter being more easily recognized. The symptoms vary from evidence of mild irritation to gross changes which may result in complete paralysis of a small area or of practically the entire body. Thus, there may be monoplegias, hemiplegias, and paraplegias. Mild manifestations are loss of strength in an isolated group of muscles or the local paralysis of a single nerve or group of the first 12 nerves. The memory may be somewhat clouded, or there may be a long attack of complete unconsciousness.

The physical signs depend entirely upon the area involved, but in general they consist of changes in the reflexes, hyperesthesia, and localized weakness. In the purely vascular type, the cerebrospinal fluid may be negative in a fairly large percentage of cases. Blood findings are usually positive.

Differential diagnosis must be made from peripheral neuritis, subacute combined sclerosis (pernicious anemia), acute or chronic anterior poliomyelitis, disseminated sclerosis, brain tumor, brain abscess, amyotrophic ateral sclerosis, syringomyelia, epidemic encephalitis, Bell's palsy, migraine, postdiphtheritic paralysis, lead poisoning, chronic alcoholism, cerebral vascular accident, paralysis agitans, cerebral arteriosclerosis, epilepsy, and Jacksonian epilepsy.

Treatment consists of intravenous injections of arsphenamine with alternating courses of bismuth or mercury.

Solitary gummas may occur in the central nervous system within a few months of infection but are much more apt to develop some years later. They give all the symptoms of brain tumor or brain abscess—signs of increased intracranial pressure with optic atrophy and projectile vomiting. The localizing symptoms depend entirely upon the site of the process. Treatment is with intravenous arsphenamine, but at times operation may be necessary to reduce intracranial pressure. It should be remembered that spinal puncture may be dangerous in either brain tumor or solitary gumma.

Transverse myelitis is usually a late symptom. It is due to a partial or complete severance of the spinal cord due to pressure from the involved meninges. The symptoms are those of any accident to the spinal cord—sphincter muscle disturbances and paralysis of all muscles below this site. Both the blood and cerebrospinal fluid will usually show a strongly positive reaction. Differentiation must be made from trauma and cord tumors. Arsphenamine treatment should be pushed.

The term "neurorecurrence" describes a neurosyphilis developing during a lapse in treatment. It is usually meningeal or meningovascular or asymptomatic. The nerves most frequently involved are the first, third, sixth, and eighth.

Involvement of the third and sixth nerves usually clears up readily under arsphenamine therapy but an optic atrophy or neuritis demands energetic treatment. There has been discussion whether the Swift-Ellis treatment (described in part IV) or malaria is the better, but at the present time the fever therapy seems to be preferable. Syphilitic deafness is intractable, and it is doubtful if any case has been cured.

Neuroses of many types have been described but unquestionably the commonest type is a marked inferiority complex as the result of infection. I have seen three patients who committed suicide rather promptly after learning that they had been infected. Free discussion of syphilis, it is hoped, will remove the false sense of guilt suffered by many patients.

Conversely, public discussion of syphilis appears to have increased the amount of syphilophobia. The syphilophobe imagines he has syphilis, and blood tests and cerebrospinal examinations will seldom restore his peace of mind. The condition is very distressing, both to the patient and to the physician, and even the best psychiatrists seem unable to provide any real relief from this obsession.

Lesions of the Bones, Joints, and Bursae

Bone lesions, while still common, are encountered less frequently than they were 25 years ago. The general belief is that they are twice as frequent in the Negro as in the white. As a rule, bone lesions are late manifestations of syphilis. Exceptionally, they may appear very early. Trauma often helps to localize the lesions.

The bones most likely to be involved are those of the nose, palate, and skull, the clavicle and sternum, and the long bones of the arms and legs. The scapula, vertebrae, and phalanges are sometimes affected.

Periostitis is the commonest lesion and is due to a primary vascular change in the deep portion of the periosteum. Swelling occurs quickly, and this irritates the nerve filaments running into the bone, pain resulting.

Osteoperiostitis results from an extension of the disease into the Haversian canals. This may end in resolution, a rarefying osteitis, or a proliferative osteitis with eburnation or exostosis.

Rarefying osteitis may lead to necrosis. A gumma may develop in the periosteum, bone, or marrow, either sharply localized or diffuse in character.

Osteochondritis (epiphysitis) occurs in congenital syphilis. It is described in section 14.

The characteristic symptoms of bone or periosteal syphilis are swelling (indurated, unilateral, and localized), severe pain, absence of lymphadenopathy, and suppuration. The diagnosis can usually be made by a positive serologic reaction and roentgenologic findings.

The contour of a small portion or of a greater part of a long bone may be changed, as in the saber shins of congenital syphilis. In the skull bones, a destructive process may eat away large areas. When the vertebrae are attacked, there may be a simple periostitis or a gummatous destruction of the body of a vertebra.

The most frequent complication is an extension of the syphilitic process into the surrounding tissues. Fractures frequently occur at the site of involvement.

Diagnostic points as emphasized by Stokes and by Moore (*30*) are as follows:

1. Routine serologic test in all patients with bone or joint symptoms, especially "subacute or chronic infectious arthritis."
2. Examine patient completely—not only lesion. Look for associated skin lesions or scars.
3. Suspect tibial, skull, and shoulder girdle lesions.
4. Syphilitic bone pain is usually nocturnal.
5. X-ray indispensable in diagnosis but negative report does not exclude inflammatory lesions, especially early.
6. Do not operate or incise for diagnosis until serologic report is at hand.
7. Suspect syphilis in the "won't heal" syndrome, whether spontaneous ununited fracture or after operative interference.
8. Suspect osteitis of the skull in severe nocturnal headache—X-ray the head before extirpating foci of infection.
9. Suspect Charcot's joint in every "hypertrophic arthritis," especially of the knee.
10. Suspect early acquired or late congenital syphilis in bilateral hydrarthrosis of ankles or knees.

The following diseases are also mentioned by Moore in the same publication (p. 29) as the sort which may be confused with syphilis of the bone

Skull	Neurosyphilis.
	Brain tumor.
	Nephritis.
	Hypertension.
	Eye strain.
	Sinus disease.

Skull	Focal infection.
	Metastatic neoplasm.
	Paget's disease.
	Xanthomatosis.
	Multiple myeloma.
	Tuberculosis.
	Actinomycosis.
Nasopalatine bones	Nose picking.
	Operative interference.
	Chrome poisoning.
	Neoplasm.
	Tuberculosis.
	Vincent's angina.
Shoulder girdle	Tuberculosis.
	Neoplasm.
	Aneurysm.
	Angina pectoris.
	Old fracture.
Long bones	Nonspecific periostitis.
	Pyogenic osteomyelitis.
	Tuberculosis.
	"Neuritis."
	Sarcoma.
	Paget's disease.
	Ununited fracture.

Joint disturbance is common in syphilis. The joints most affected are knees, hips, shoulders, elbows, ankles, and wrists, in that order. It is now known that the trouble is due to the presence of the spirochete at the site. In early cases, trauma does not appear to play a significant role in localizing the trouble, but injury frequently precedes the joint involvement in late cases. Joint syphilis may be classed as follows:

1. Early—
    a. Arthralgia.
    b. Synovitis.
    c. Hydrarthrosis.
2. Late—
    a. Arthralgia.
    b. Synovitis.
    c. Hydrarthrosis.
    d. Osteochondro-arthropathies.
    e. Gummatous perisynovitis.
    f. Charcot's joint of tabes.

The arthralgias are the simplest and most frequent joint involvements of syphilis. They occur early, usually with the secondary rash. The large

joints are most likely to be affected. Roentgen-ray examination reveals no joint abnormality.

Synovitis is of three types, acute, subacute, and chronic. The acute type is most frequent during the first year of infection, but may occur during any stage of syphilis. The condition simulates acute rheumatic fever, the joint being red, swollen, and painful; there is often high fever. Synovitis is usually confined to one joint. Roentgen-ray examination reveals no changes.

Subacute synovitis is simply less severe. There is considerable doubt that the chronic type is due to syphilis. It is never associated with effusion.

Hydrarthrosis, or arthritis with effusion, caused by syphilis usually occurs before the third year of infection and is generally believed to be uncommon. The knees, elbows, wrists, and ankles are the joints most frequently involved. The onset tends to be insidious, the first symptoms being discomfort and swelling. The skin appears normal, and there is no muscle atrophy. The head of the bone is almost constantly painful. The serologic reaction of the joint fluid is positive. Laboratory examination of the fluid is necessary for early differentiation from tuberculosis.

Osteochondro-arthropathies are due to destructive or proliferative gummatous changes in the vicinity of the joints. They occur only during the late stages of syphilis. The knees, shoulders, elbows, and wrists are affected in that order of frequency. The disease runs much the same course as tuberculosis, from which it may be distinguished by roentgenograms and laboratory tests.

Gummatous perisynovitis is rare. It usually affects the large joints. No bone changes can be detected by X-ray.

Treatment of bone syphilis is identical with that of syphilis in general.

Tabetic arthropathy, also known as Charcot's joint, comes on either early or fairly late in the course of tabes dorsalis. The general belief is that the condition is a disintegration due to a loss of innervation, which in turn results from syphilitic infection of the central nervous system. This viewpoint is supported by the finding of an analagous condition in syringomyelia. Yet, careful roentgen-ray study of the affected joints of syphilitics in most instances reveals positive signs of syphilitic lesions. In the majority of cases only one joint is involved. The greater frequency of the condition in knee, ankle, or hip suggests that the stamping gait of tabes may be responsible. At times, however, a number of joints may be involved. Antisyphilitic treatment has little effect, but should certainly be given for the benefit of the tabes. Various types of braces have been used by the orthopedist with benefit.

Syphilitic bursitis has been fully described by Churchman (*58*). The picture is usually that of indolent swelling of the bursae, most frequently in the knees. Gummatous changes with ulceration occur. Any long-continued swelling of the bursae should be investigated for syphilis.

Syphilis of the kidney may occur at any stage of the disease. Acute syphilitic nephritis is an early complication and is comparable to nephritis following any of the acute infectious diseases. It closely resembles post-scarlatinal nephritis. Syphilis may also attack the kidney in late stages, giving rise to such pathologic changes as interstitial degeneration, amyloid degeneration, and gumma. Kidney involvements may be classified as follows:

1. Secondary stage—
    a. Transient albuminuria.
    b. Acute and subacute nephritis—preroseolar nephritis.
2. Tertiary stage—
    a. Chronic interstitial and parenchymatous nephritis—contracted kidney (Schrumpfniere).
    b. Amyloid kidney.
    c. Gumma of kidney.
3. Congenital syphilis—
    a. Early nephropathies.
    b. Late lesions.

A transient albuminuria may appear about the time that the secondary eruptions begin. Casts are never present. The albumin disappears rapidly under antisyphilitic treatment.

Acute or subacute syphilitic nephritis takes place at any time after the initial lesion. The urine exhibits a considerable amount of albumin, while casts, red blood cells, and leukocytes also are usually present. The presence of lipoids in the urine is highly suggestive of syphilis. There is usually marked edema. The deciding diagnostic factor is apt to be a therapeutic test with arsphenamine. The disease must be distinguished from kidney damage due to treatment.

Mercury is contraindicated in this condition, and bismuth hardly to be recommended. Under arsphenamine treatment, the disease improves slowly.

Chronic parenchymatous and interstitial nephritis may at times be due to an antecedent syphilis. The disease develops at a late stage of syphilis. Polyuria is not as rare as in the nonsyphilitic form; the urinary sediment is small in amount; albumin is abundant; marked anemia is rather characteristic. The serologic reaction is positive. Some improvement may be obtained by antisyphilitic treatment in subacute cases if extensive degenerative changes have not taken place.

Amyloid degeneration of the kidney is recognized as sometimes being due to syphilis. It is considered to be the result of a long-continued toxemia associated with chronic forms of the infection. The patient often manifests

[3] This section is taken for the most part from the chapter by H. A. Fowler, M. D., Washington, D. C., in my textbook on syphilis.

rather late lesions, is anemic, has poor digestion, and may have an edema of the face or ankles. The urine contains abundant albumin, but rarely does the arterial tension increase. Both liver and spleen are frequently enlarged. The condition is resistant to any type of treatment.

Gummas of the kidney are almost always multiple, ranging from a hazelnut to a walnut in size. The whole organ may be involved in a single large tumor. Gummas are often present in other organs. Arsphenamine treatment usually removes evidences of the disease, although kidney scars persist.

Probably about 50 percent of the cases of paroxysmal hemoglobinuria are associated with syphilis, particularly the congenital form.

The only syphilitic condition in the bladder or prostate frequent enough to merit mention results from tabes. The patient encounters difficulty in urination, and elimination is incomplete. Cystoscopy reveals these changes: (1) Trabeculation, (2) relaxation of the vesical outlet, and (3) elevation and hypertrophy of the trigone. The trabeculae consist of a fine interlacing network of muscle bundles and are particularly well-marked at the base and on either side of the trigone. The treatment is that for tabes, but decided improvement may be obtained from regular catheterization and careful, continued local treatment of the bladder.

Syphilis of the testicle is frequently found at autopsy. Clinical manifestations are rare in the white but rather frequent in the Negro. In contrast to tuberculosis, the disease usually involves the testicle primarily and the epididymis secondarily. Two forms of the affection are recognized—diffuse interstitial sclerosis and gumma. The two processes usually occur together, but gummas receive more attention in the clinic because interstitial sclerosis causes the patient little difficulty. Gummatous orchitis develops slowly as a rule but may be acute. The swelling may become 3 or 4 inches in diameter. It is hard and heavy. Subjective symptoms are usually absent. It may be difficult to differentiate this condition from a tumor of the testicle. Serologic examination is, of course, helpful, and the therapeutic test is final. While the prognosis is good, some atrophy always results and the testicle may cease to function. Many excellent surgeons believe that the growth should be removed if treatment is not completely effective.

The vagina, uterine body, fallopian tubes, and ovaries are rarely affected. It may be noted, however, that it is possible for the female breast to become acutely inflamed, diffusely swollen, and painful during the early eruptive period. Localized gumma of the breast is distinctly rare, and when it occurs tends to break down rapidly, which differentiates it from cancer.

Syphilis of the Eye

Syphilitic iritis may occur as early as 6 weeks after the initial lesion appears. It cannot be differentiated clinically from an iritis caused by rheumatism, gonorrhea, tuberculosis, and focal infection save by laboratory investigation.

There is one form of syphilitic iritis which presents certain well-defined clinical signs that should immediately suggest syphilis to the examiner. This is the iritis papulosa. Here there is a high degree of injection of both conjunctival and ciliary vessels. The iris is discolored and its pattern obscured to a mild extent. Examination with oblique illumination reveals the presence of nodules which are usually situated at the pupillary border of the iris. These are yellowish red or brown in color and about pinhead in size.

Acute iritis is a medical emergency requiring immediate application of a mydriatic to prevent adhesion of the iris to the lens. Steps should then be taken to make a definitive diagnosis of the cause of the iritis, a blood test for syphilis being included. If syphilis is found, antisyphilitic treatment should be added to the local therapeutic measures. The local therapy is best administered by an ophthalmologist.

Syphilitic choroidoretinitis is most frequently encountered between the fourth and twentieth months of the disease, although it may not appear until later. Both eyes are usually affected, and the disease runs a chronic course. The symptom which first attracts the patient's attention is the diminution of visual acuity. There is also a distortion of objects due to the displacement of the rods and cones of the retina. The appearance of the eye grounds and media on ophthalmologic examination confirms diagnosis. Prognosis must always be guarded.

The optic nerve may be affected throughout its entire course, or any part may be the seat of the inflammatory process. Optic neuritis is by no means always caused by syphilis, but this infection is outstanding as one of the most frequent causes. The intracranial portion of the nerve is affected most commonly, for here it may be attacked by gumma or by extension of gummatous infiltration from the meninges. The neighborhood of the optic chiasm is a favorite site for meningitis. A differential diagnosis cannot be made absolutely by the ophthalmoscopic picture, although there may be a characteristic thickening of the retinal vessel walls.

Papillitis, or inflammation of the intraocular portion of the nerve, manifests itself externally by no sign save that the pupils are dilated in proportion to the diminution or absolute loss of vision. The ophthalmoscope shows increased redness of the disk, an indistinct margin, an alteration of the retinal vessels with small arteries (which may or may not be tortuous) and congested veins and hemorrhages.

Choked disk is most frequently caused by brain tumors, but syphilis cannot be disregarded, particularly a moderately large gumma.

Atrophy of the optic nerve may be primary or secondary. Any of the conditions just mentioned may have, as their termination, atrophy. In from 40 to 50 percent of cases of progressive primary atrophy, tabes is the etiologic factor. As already mentioned the best treatment for primary atrophy is probably malarial inoculation, although Swift-Ellis treatment is also used.

Interstitial keratitis will be discussed in the section on congenital syphilis.

In dealing with the subject of congenital syphilis much trouble will be avoided if we remember that congenital syphilis is caused by an infection with the same organism that is found in acquired syphilis and that the results of this infection are very similar. For this reason it is possible to write briefly concerning the symptoms and pathology of the disease.

Infection is almost universally conceded to be placental in origin. Even if the seminal fluid were infectious as Boardman (*59*) and, more recently, Kertesz (*60*) have contended, this still does not prove that children are infected through such an agency, inasmuch as it is difficult to believe that an ovum containing a treponeme could develop. Recent experimental work of Kemp (*61*), however, indicates that the semen of men with late syphilis is not infectious.

A syphilitic placenta is much larger than a normal one. Frankel called attention to the changes in the chorionic villae in 1873. When they are teased out in salt solution they are seen to have become much thicker and more club-shaped than is normal. Microscopically there are characteristic syphilitic changes in the blood vessels, and the stroma cells are closely packed instead of being stellate.

The frequency of congenital syphilis has been discussed in the section, "Prevalence of Congenital Syphilis." The Cooperative Clinical Group has definitely established the fact that 84 percent of all pregnancies in untreated syphilitic women end in disaster, either intrauterine death or the birth of a syphilitic child.

The clinical course of congenital syphilis is sharply divided into two great groups: one showing early manifestations, and one not showing lesions until the age of puberty or later. Fournier has directed particular attention to the latter, calling it syphilis hereditaria tarda. In reality while this classification may be useful clinically yet pathologically it is analogous to acquired syphilis, for as has already been emphasized it is not unusual to find that after a very mild early course severe late lesions may develop after the lapse of many years.

For years it has been the custom to blame various malformations in the child on the effects of syphilis. For instance flat foot, scoliosis and various other of the bone deformities, congenital heart disease, hernia, deafmutism, malposition of the viscera, and many other troubles have been laid at the door of syphilis. Now as a matter of fact a child is either syphilitic or not syphilitic, and it is extremely improbable that any of these dystrophies are caused by syphilis. It is usual for the syphilitic manifestations to appear shortly after birth; ordinarily, the child when born appears healthy.

The lesions seen early in the course of congenital syphilis do not differ materially from those seen in the same stage of acquired syphilis. There is usually an eruption, mucous patches, some glandular enlargement, condylomas, and frequently a marked alopecia on the back of the head where it has rubbed on the pillow. There are a number of other features, how-

ever, that must be considered. There is usually more systemic disturbance than is found in the acquired type of the disease; the child rapidly becomes poorly nourished and is frequently very fretful. Very often there is a marked rhinitis that gives rise to "the snuffles." The face often looks drawn and pinched, and there may be rhagades from the corner of the mouth. A little later gummatous changes may develop in any organ. The bone changes are somewhat different from those occurring in acquired syphilis and will be described further in this section. Dactylitis is more common. At times no early manifestations will be noted and gummas will be the first lesions observed; they rarely appear before the child is 2 years of age.

The early cutaneous lesions of congenital syphilis are very similar to those already described in the section, "Early Cutaneous Syphilis." Vesicular lesions are rare, although they may occur in connection with bullous lesions. Bullous lesions, the syphilitic pemphigus, are not as common a the majority of textbooks would have us believe. In over 600 cases of congenital syphilis I have encountered this condition only three times. The bullae are most common about the hands and feet and the adjacent portions of the limbs but may occur upon any portion of the body. In size they may reach well over an inch. They may be either distended or flaccid, and the contents may be either clear or cloudy. The base is usually raw. They are frequently surrounded by an inflammatory areola. Such lesions must be distinguished from both pemphigus and bullous impetigo, and the clinical diagnosis may depend upon finding other manifestations of syphilis, usually not a difficult procedure. Condylomas are frequently found about the perineum and anal region and may reach a very considerable size.

The late cutaneous lesions of congenital syphilis are comparable to the lesions developing in the course of late acquired syphilis. The gummatous lesions, however, are the most common. It is rather unusual to see the serpiginous nodular lesions that are so often encountered in the acquired type of the disease. The destruction resulting from ulcerating gummas is often very extensive, and the lesions may be extremely intractable to treatment. Squamous syphilids of the palms and soles are very rare.

Affections of the mouth and throat are to all intents and purposes identical with those of persons with acquired syphilis. There is one notable exception, however, namely, the fact that the teeth of a congenital syphilitic show certain characteristic changes. The typical Hutchinson's teeth of congenital syphilis are the upper middle incisors of the second or permanent set (Figure 13, page 95). Typical teeth have a single notch in the center. The tooth is usually small both in length and width and is not flattened out as is normal, but is peg-like, or rounded. Still (*62*) reported similar changes in the canine teeth in one case. Stokes has been able by means of the roentgen ray to recognize changes before eruption. The mulberry molars of Fournier or Moon are the 6-year upper and lower molars. The characteristic change is an erosion of the grinding surface,

which is irregular in form so that this surface becomes pitted, excavated, and discolored. The supernumerary tubercle of Carabelli has been proved to have no diagnostic significance.

Syphilitic coryza is frequently manifested shortly after birth—the child develops snuffles. This is a purulent rhinitis that often becomes offensive. The child has a peculiar snorting inspiration and frequently holds the head back to aid in respiration. Suckling is always interfered with. Still claimed that coryza is present in 70 percent of the cases. The upper lip often becomes eroded, and the mucous membranes of the nose may become permanently atrophied. This form of syphilis does not lead to saddle nose which is always due to gummatous changes. The gummatous lesions are in no wise different from those of tertiary acquired syphilis.

Hepatic syphilis is extremely common in congenital syphilis. Rolleston (*63*) considers that there are three main types, that occurring at the same time that the secondary manifestations appear, the tardive type, and the multilobular cirrhosis that supervenes in later life. In the first type the child may be born healthy and the lesions develop rapidly or the child may be stillborn. There are usually signs that point to liver disease, such as an enlarged liver, although jaundice and ascites are frequently absent. The liver is firm and tender; at times there is a localized tumor formation, but this is rare. The spleen is frequently enlarged as well. When jaundice does occur it may be due to secondary infection as Milon (*64*) pointed out. Pathologically the changes are usually diffuse; the surface may show adhesions, but usually the surface is smooth.

Syphilitic disease of the cardiovascular system is unusual in congenital syphilis.

Myocardial syphilitic lesions were well described by Warthin (*65*) on a basis of 50 cases that he had studied. He divided the lesions into parenchymatous and interstitial, just as in the cases of acquired cardiac syphilis. Other observers have reported the presence of true gummas in the heart muscles of congenital syphilitics.

Aortitis may be induced by *Treponema pallidum* in congenital syphilis, as Klotz (*66*) has shown.

The blood shows a marked secondary anemia in connection with congenital syphilis. It is usually stated that a high lymphocyte count is the rule, but I (*67*) have been unable to confirm this finding; only one of my five cases showed a high count.

Syphilis of the spleen is common in congenital syphilis and has been recognized since the publication of S. B. Gee's paper in 1867. Still (*62*) stated that it is easily palpable in 45 percent of the cases and at least one inch below the costal margin in 22 percent. There are three types of lesions the simple hyperplasia, the diffuse fibroid changes due to miliary gummas, and the true gumma, examples of which have been reported.

Syphilis of the lymph nodes is considered to be less common in congenital syphilis than in acquired syphilis, a point with which I thoroughly agree.

During the early stages, however, it is usually possible to find a number of such nodes, and in almost every case I have found that the epitrochlear nodes were palpable. This at times may be a valuable diagnostic point.

Syphilis of the bones is frequently encountered (*68*). While osteochondritis (epiphysitis) is unquestionably the characteristic osseous lesion of congenital syphilis, still periostitis and osteitis do occur and not rarely. Dactylitis is also fairly common.

Periostitis may occur at practically any stage of the disease and is in reality a counterpart of the type found in the acquired form, although there may be rather more deformity. The tibias are probably more frequently affected than are any of the other bones, and the well-known "saber shins" may result, they being due to a marked convexity of the anterior edges (Figure 14, page 96). The usual course of the disease is for the subperiosteal gummas to calcify, but ulceration to the exterior may result.

Osteitis and osteomyelitis are similar to the conditions already described in the section on syphilis of the bones. However, the skull bones are not so frequently affected, while the nasal bones are more frequently involved. Parrot, in 1886, described bossing of the skull as due to syphilis. A typical textbook case should show four thickened, rounded elevations at the vertex of the skull surrounding the anterior fontanelle; at times, only two are present. Coutts believed that four bosses indicate syphilis, but Still did not concede this point. Rickets may cause a similar condition.

Dactylitis is not infrequent. Still gave an incidence of 2 percent. In the vast majority of instances it occurs before the age of 2 is reached. The proximal phalanges of the fingers are usually affected, but the toes may be involved and in one or two cases the metatarsals have been affected. Clinically there are usually several fingers involved, and the disease may be unilateral or bilateral. A fusiform swelling slowly develops, and it is unusual for this to soften or break down. The condition has been variously considered as due to epriostitis, epiphysitis, osteitis, or osteomyelitis. It must be distinguished from tuberculosis, and here the age of the patient as well as the various clinical and laboratory signs will aid in making a correct diagnosis.

Osteochondritis was first described by Wegner in 1870. Three types of lesion occur. The most characteristic and typical occurs along the line of ossification; the single line of demarcation becomes thickened and enlarged. In advanced stages a subluxation may occur. In addition there is frequently some periostitis and also certain changes in the marrow, which may be responsible for the anemia that sometimes accompanies congenital syphilis. Osteochondritis frequently results in the stunted growth of the long bones. The pseudoparalyses of Parrot are not infrequent accompaniments of the disorder. Usually there is considerable tenderness on pressure and the child cries when handled. This form of osseous syphilis is far from uncommon. Still stated that it occurs in from 11 to 22 percent of all cases.

It should always be remembered that it is more than possible that certain other diseases of the bones, such as rickets, may at times give a picture which the roentgenologist will be unable to distinguish from congenital syphilis. Also, if the mother has received bismuth therapy during pregnancy a roentgenologic picture may be produced which is difficult to distinguish from certain lesions of congenital syphilis.

Syphilis of the joints is far from rare. Arthralgia naturally cannot be well recognized in young children, but tenderness on pressure may give a clue. Hydrarthrosis was first described by Clutton (*69*) and frequently goes under the name of "Clutton's joints." The majority of writers on congenital joint lesions now recognize them as a distinct type of congenital arthritic syphilis. These joints usually develop in early adolescence; the only sign or sympton is the presence of fluid in the joints. The knees are most frequently affected, and the effusion is frequently bilateral. The synovial membrane is the site of diffuse gummas. Treatment is usually prompt in its results.

Lesions of the kidney usually occur in association with specific lesions and congenital deformities of other organs and parts of the body. Fournier states categorically that kidney diseases are common in congenital syphilis.

Congenital neurosyphilis is very similar to acquired neurosyphilis. Juvenile paresis and tabes, meningitis, and vascular neurosyphilis are the most frequent forms, but pure myelitis is very rare. In 28.8 percent of Kingery's 52 cases of congenital syphilis there were abnormal changes in the spinal fluid (*70*).

There are a number of clinical pictures which are more or less characteristic—certain forms of feeble-mindedness, hydrocephalus, ependymitis, Friedreich's ataxia, primary optic atrophy, Little's disease, a nervous form of rickets, simple nervousness, amaurotic family idiocy, and epilepsy.

Juvenile paresis was first described by Clouston in 1877. The disease is not especially frequent, but many cases have been reported. The first symptoms are usually shown about the time of puberty. The symptoms, course, and treatment are similar to the ordinary forms. As a rule it does not respond to treatment as readily as does the acquired form.

Juvenile tabes is very rare, and is hardly worth description, as it is practically identical with the acquired form.

A diffuse cerebrospinal syphilis is common and identical with the adult form.

While a precocious child is sometimes found, feeble-mindedness is much more common. Although a general agreement on figures is lacking, there seems no doubt that many syphilitic children are mentally much retarded.

Idiopathic epilepsy has no relationship to syphilis. A syphilitic epilepsy should be of the Jacksonian type, but this is not always true; I have seen several cases which rather closely resembled idiopathic epilepsy but were due to a congenital neurosyphilis. At the same time it must be remembered that the two diseases can coexist.

Hydrocephalus is not uncommon in congenital syphilitics and is usually due to an arteritis. The usual time of onset is from the third to the eleventh month. A few cases have been reported as cured by antisyphilitic treatment.

Sachs has described a symptom complex consisting of dementia, spastic paralysis of the extremities and failure of vision, which appears in several members of the same family. Some of the reported cases are certainly syphilitic in origin. (Nonne, Spielmeyer.)

Occasionally there develops the symptom complex of spastic symptoms, convulsions, and paralyses which cannot be differentiated from a true Friedreich's ataxia.

In congenital syphilis a picture of neurogenic rickets appears. Convulsions usually occur.

The diagnosis must be made by spinal fluid examination just as in acquired neurosyphilis.

The prognosis is apt to be bad, for in many instances the disease is not recognized until late. Smith (*71*) in his review of congenitally syphilitic children treated at Johns Hopkins Hospital states that all forms of congenital syphilis yielded readily to treatment except neurosyphilis.

The treatment is identical with that of acquired neurosyphilis.

Sociologically much needs to be done. The mental defectives need special care and training, and the advanced cases need institutional care of a better kind than is usual, for intelligent and persistent treatment combined with vocational training may make some useful citizens.

Interstitial keratitis is the most common symptom of congenital syphilis in children between the ages of 5 and 16, although it may appear earlier or later. It is looked upon as essentially due to congenital syphilis, yet, at times, it is seen in the acquired type. The disease usually begins gradually with slight ciliary congestion followed by the appearance of one or more faint cloudy patches usually near the center of the cornea. Upon examination these are seen to be within the corneal structure. These gradually spread and fuse until the entire cornea becomes lusterless and dull. Blood vessels derived from the ciliary vessels begin to make their appearance in the corneal structure, producing a dull, reddish yellow appearance, giving rise to the characteristic salmon patch. After the disease has reached its height, it begins to subside, the cornea clearing from the margin towards the center and frequently leaving permanent opacities which interfere with vision.

Iritis is always associated with interstitial keratitis and occasionally chorioretinitis. The disease is bilateral, and whereas the second eye may become involved shortly after the first, yet as much as a year has elapsed before it has made its appearance. The subjective symptoms are diminution of vision, pain, lacrimation, and photophobia.

Most opthalmologist have finally become converted to the correct view that arasphenamine is of marked benefit in interstitial keratitis. Recently

riboflavin has been used as auxiliary treatment, with success in some cases.

Prenatal syphilis should be suspected when syphilis has been discovered in the father, mother, brothers, or sisters. It is well known that physical examinations in pregnant women very frequently reveal no signs of the disease with the single exception of positive serologic findings. Every pregnant woman should be examined for syphilis early in the course of pregnancy and again 3 or 4 months later. It is a well-known fact that an untreated syphilitic woman has only a 16-percent chance of bearing a normal, living child. The birth of syphilitic babies is preventable at least 9 times out of 10. Congenital syphilis is as great a disgrace to modern medicine as is typhoid fever.

Congenital syphilis can be found if the following procedures are practiced:

1. Suspect every baby of known syphilitic mothers whether treated or not before or during pregnancy.
2. In such children do—
    a. Dark-field examination of scrapings from wall of umbilical vein.
    b. Roentgenogram of infant's long bones at 2 weeks.
    c. Blood test at 2 weeks.
    d. If these are negative, serologic follow-up monthly for 6 months; every 6 months for 2 years.
3. In babies, suspect syphilis in—
    a. Puny, ill-nourished, wizened, "won't gain" infants.
    b. Skin rashes of any type.
    c. Snuffles.
    d. "Pseudoparalysis." Check suspicion by routine serologic test.
4. In older children and adolescents, suspect syphilis, especially:
    a. "Pink eye" (interstitial keratitis).
    b. Deafness unless clearly middle ear.
    c. Hydrarthrosis of the knees (Clutton's joints).
    d. Osteomyelitis.
    e. Peculiar second dentition. Check suspicion by routine serologic test.

Roentgen-ray examination of an infant's long bones at 2 weeks of age is much more important than it is some months later, for the reason that other diseases may produce practically an identical picture. A blood test at 2 weeks is not conclusive unless supported by definite clinical lesions, inasmuch as Cregor and Dalton (*72*) have shown that the blood of certain healthy infants, born of syphilitic mothers with positive tests, is occasionally positive for the first 10 days to 3 weeks only to clear up at a later date and remain clear. Conversely, in an infant whose blood is at first

negative a positive serologic reaction may develop later. Not all cases of snuffles are due to syphilis, for colds of various types are not uncommon.

The physician must always remember that, when he finds a child with congenital syphilis, it is his duty to examine the rest of the family both clinically and serologically.

The treatment of congenital syphilis should approximate that of acquired syphilis, but there are a number of important differences. In early cases the veins are usually so small that intravenous injections are difficult, and in some later cases treatment must be prolonged. Moore well portrays the procedure for treatment of infants.

Suggested outline of treatment for early congenital syphilis [1]

Week	Drugs	Dose	Remarks
1.....	Sulfarsphenamine.....	5–10 mgm/kg...	Test blood Wassermann. Avoid therapeutic shock.
2–7.....	Sulfarsphenamine.....	25 mgm/kg.....	
8–11.....	Mercury by inunction daily.	1–2 gm.....	
	or		
	Bismuth salicylate weekly.	2 mgm/kg.....	
12–19.....	Sulfarsphenamine.....	25 mgm/kg.....	Test blood Wassermann. *Do not stop treatment when Wassermann becomes negative.*
20–25.....	Mercury or bismuth....	.....	
26–33.....	Sulfarsphenamine.....	25 mgm/kg.....	Test blood Wassermann. Also test spinal fluid at about this time.
34–41.....	Mercury or bismuth....	.....	
42–49.....	Sulfarsphenamine.....	25 mgm/kg.....	Test blood Wassermann. Note gradual lengthening of heavy metal course: 4, 6, 8, and now 10 weeks.
50–59.....	Bismuth or mercury....	.....	
60–67.....	Sulfarsphenamine.....	25 mgm/kg.....	Test blood Wassermann.
68–79.....	Bismuth or mercury....	.....	This is absolute minimum of treatment, which should be continued longer, if necessary, to fulfill serologic standard.
80–132....	Probation. No treatment.	.....	Test blood Wassermann every 2 months. Test cerebrospinal fluid at end of year.
Thereafter.	Prolong follow-up with physical and blood Wassermann reexaminations every 6–12 months until puberty is passed; and if possible thereafter at least until early adult life is reached.		

[1] From Dr. J. E. Moore's book, "The Modern Treatment of Syphilis." Courtesy of Charles C. Thomas, publisher, Springfield, Ill.

Sulfarsphenamine can be given safely to infants by the intramuscular route. Under no circumstances should the attempt be made to inject neoarsphenamine into the longitudinal sinuses (by way of the anterior fontanelle) as death has resulted in a number of instances. The sulfarsphenamine should be given in a 33⅓ percent solution into the upper and outer quadrant of the buttock, under the gluteous maximus muscle; the dosage should be in accordance with the weight of the child.

Either mercury or bismuth may be employed as the heavy metal. Bismuth should be administered intramuscularly; mercury may be given in the same manner. Mercury may also be given in inunctions using a 50-percent mercury ointment. This is probably preferable in undernourished children. The dose is one gram daily, placed on the inner surface of an abdominal binder and allowed to remain in position at least 12 hours out of each 24. Mercury by mouth is apt to cause digestive disturbances.

Iodides are unnecessary. Stovarsol (acetarsone) is not advised; my experiences with it have not been fortunate.

Fortunately the late forms of congenital syphilis are not transmissible so do not form a public-health problem; the one problem is to prevent the development of complications, especially interstitial keratitis and nerve deafness.

The treatment of interstitial keratitis is both local and general. Locally atropine or dionine is employed; dark glasses and the avoidance of eye work are essential. Treatment should be begun early. The general treatment consists of alternating courses of arsphenamine and bismuth. The succinimide of mercury may be given three times a week during the arsphenamine course. The active inflammatory lesions yield in from 6 to 16 weeks but often leave corneal opacities. Treatment should be continuous for 2 years. In very obstinate cases either malaria or typhoid injections may be tried; they often give excellent results.

One last word: The serologic reaction in the late type of congenital syphilis is usually irreversible; do not be disturbed by its persistancy but do not continue to treat indefinitely.

Part III

Diagnosis

Examination of Patient

Syphilis is frequently spoken of as "the great imitator." Unless great care is taken, syphilis is often mistaken for other diseases, and other diseases mistaken for syphilis. Some conditions even have the temerity to give serologic reactions that are identical with those found in syphilis. The clinical signs and symptoms of the disease may be very slight and in latent syphilis totally lacking. Unfortunately too many physicians still feel that "syphilis does not occur in nice people," an attitude that leads to much difficulty, for the spirochete is no respector of titles, of wealth, of breeding, or of education. Blood tests for syphilis should be performed routinely on all patients by all physicians whether syphilis is suspected or not. Failure to suspect syphilis is due to stupidity or prejudice, but "snap diagnoses" of syphilis are little short of criminal; the diagnosis should be made rapidly but carefully, just as is the diagnosis of acute appendicitis. The physician needs to know a reliable place where he can have dark-field examinations and serologic tests done. He is probably acquainted with a roentgenologist and an ophthalmologist; let him also consult freely with a syphilologist. The following will show the nature of the various diagnostic procedures:

1. History—
    a. Personal.
    b. Family.
    c. Associates.
2. Clinical examination—
    a. Genitalia and perineum.
    b. Skin and hair.
    c. Mucous membranes.
    d. Bones, joints, and bursae.
    e. Lymph nodes and spleen.
    f. Liver.
    g. Eyes.
    h. Hearing.
    i. Teeth.
    j. Respiratory tract.
    k. Cardiovascular system.
    l. Neurologic and psychiatric.
    m. Cystoscopic.
    n. Therapeutic test.

3. Laboratory examination—
    a. Dark-field.
    b. Lymph-node puncture.
    c. Blood-serum tests.
    d. Spinal-fluid tests.
    e. Histologic.
    f. Roentgen-ray.

The personal history of patients must always be accepted with much caution for some will attempt to deceive the physician, and others may not understand the questions asked of them. Some will magnify and some will minimize affections. Even with careful questioning it is frequently difficult to obtain a satisfactory history. In addition it is a well-recognized fact that the signs and symptoms of the initial and secondary stages may be so slight that it is natural for the disease to be unsuspected by the patient.

The history of family or associates may or may not be helpful for the reasons that have already been mentioned. Naturally, a family history is taken when one suspects congenital syphilis. It is a good practice invariably to ask whether the wife has had any miscarriages and to find out about the early history of the children. Suspect syphilis when there is a history of stillbirths or miscarriages occurring in the third trimester of pregnancy.

Examination of the family or associates may or may not throw considerable light on the case in question. If a mother has active syphilis, the child may reasonably be suspected of having the disease. The existence of syphilis in one of a married couple should lead us to search for it in the other. At the same time it is often surprising how a person can escape infection even after repeated exposure. In the old days we heard much of "diagnosis by confrontation." A man who has a lesion after having consorted with a woman who has a definite active syphilitic lesion has good reason to suspect that he has acquired syphilis. At the present time this method is not used as the final criterion.

Thorough inquiry should be made in regard to sexual contacts. This is of great value, not only in establishing the patient's diagnosis but also in revealing and bringing to treatment additional cases of syphilis, thus retarding the spread of the disease in the community. If extragenital infection is suspected inquiry should also be made in regard to additional close or intimate contacts.

Clinical examination of the genitals must never be neglected. Ordinarily the scar of a chancre is small, but this is not necessarily the case. In the female, the cervix should never be neglected. The mere existence of a scar upon the genitals does not make the diagnosis of syphilis certain, for it may be due to a chancroid, various superficial diseases, or trauma. Always examine the scrotum for a nodular eruption and perineum for condylomas or radiating lines.

Examination of the skin and hair is extremely important and should always be done in a good light either from a window or from a blue electric

light bulb. In ordinary artificial light a faint roseola is often overlooked. During the fulminating stage an experienced dermatologist can frequently make a tentative diagnosis of syphilis at a glance. In the late stages the annular, nodular eruptions are characteristic; and ulcers are always suggestive of broken-down gummas. The patchy character of syphilitic alopecia is quite characteristic. Final diagnosis, however, should never be made until the laboratory data are at hand. If these fail to confirm the clinical diagnosis a therapeutic test is sometimes justified.

Examination of the mucous membranes of the mouth and nose may reveal signs of syphilis. Mucous patches are common, although they may be imitated by the lesions of Vincent's angina, herpes, and erythema multiforme. In the late stages, scars of destructive processes may be present. Most common are perforation of the nasal septum or palate and deformities of the pillars or the uvula.

Examination of the bones, joints, and bursae, especially the tibiae, clavicles, and frontal bones should be routine. Nodes can arise from causes other than syphilis, but this is rather infrequent. The sternoclavicular articulation should never be overlooked, since a swelling at this point is very suggestive of syphilis. All joints should be tested for motility, tenderness, and swelling. Broken-down bursae are extremely suggestive, and even a chronic proliferative bursitis must be regarded with grave suspicion.

Examination of the lymph nodes and spleen may be richly rewarded. The following sets of nodes must always be palpated: Posterior cervical, anterior cervical, submental, axillary, anterior axillary, epitrochlear, and inguinal. Bilateral enlargement of the posterior cervical and epitrochlear nodes is very suggestive of the presence of syphillis. The spleen and liver may be enlarged during secondary syphillis and early congenital syphilis.

Examination of the eyes is fourfold in character: First, of the extrinsic muscles; second, of the cornea and sclera; third, of the pupils; and fourth, ophthalmoscopic examination.

Both ptosis and an acquired internal strabimus are always very suggestive, and a simple weakness of the eye muscles may be of some value to the diagnostician. Inspection for interstitial keratitis or scars therefrom, iritis, or choroiditis is of the utmost importance. Irregularity, unequal size, and miosis of the pupils are suggestive of neurosyphilis just as is failure of the light reflex.

Every syphilologist should be able to recognize any grave changes in the retina or optic nerve by means of the ophthalmoscope, but it is always well to refer any suspected eyes to the ophthalmologist.

Examination for hearing should never be neglected. Sudden total deafness is not uncommon in syphilis though often there is a prelude even to this, and slowly developing deafness is by no means unknown in either the congenital or acquired form of the disease.

Examination of the teeth has diagnostic significance only in congenital syphilis and this has already been discussed.

Examination of the respiratory tract is important. Hoarseness is not infrequent during any stage of syphilis and its presence should always be noted.

Cardiovascular examination often reveals late syphilis. Recognizing a tympanitic (tambour) quality of the aortic second sound is just as important as the fluoroscopic discovery of an aneurysm. Aortitis, aortic insufficiency, and aneurysm are usually due to syphilis, while angina pectoris in persons under 40 and some cases of myocarditis are very suggestive.

Neurologic examination only too often reveals the presence of late syphilis. As already indicated it must include examination of the pupils and eye muscles and of the biceps, triceps, abdominal, cremasteric, patellar, and tendo achillis reflexes. Tremor of the extended tongue and fingers must be noted, and the presence of a negative or positive Romberg sign shown. Always test for coordination. In talking to the patient notice his train of thought, emotional responses, and speech. Tests of memory and judgment and having him repeat test phrases may be helpful. A more complete neurologic and psychiatric examination is often desirable.

Cystoscopic examination not infrequently reveals a trabeculated bladder which usually occurs with tabes, although it may be found in other diseases of the cord. This examination should be made when indicated.

Therapeutic Test

The therapeutic test is occasionally necessary in order to establish a satisfactory diagnosis. It should be used only as confirmatory evidence or as a last resort when other diagnostic methods fail. It is especially valuable in suspected malignancy developing on a syphilitic tongue but may likewise be of use in differentiating between carcinoma and syphilis of certain viscera.

When malignancy is suspected, injections of arsphenamine should be given twice a week; if a satisfactory change does not occur within 3 weeks, it is generally safe to assume that the condition is not syphilis. With respect to skin lesions remember that arsenic often has a nonspecific healing effect on nonsyphilitic lesions. In such cases it is better to use bismuth for the therapeutic test.

Dark-Field Examination

Dark-field examination is of use only in the early stages of syphilis; it is absolutely without value in the late stages. In the diagnosis of an early chancre it is far and away the best test, being positive in at least 90 percent of all instances. As the chancre becomes older—3 to 5 weeks—the percentage of positives decreases. In secondary syphilis it is of great value in condylomas and mucous patches, and sometimes positive serum can be obtained from the skin lesions. In intraoral lesions it should not be used for it is impossible to distinguish the spirochetes of syphilis from the normal spirochetal flora of the mouth.

It takes a certain amount of training to use a dark-field apparatus with assurance, but the average physician can either refer his patient to a competent pathologist, or obtain serum from the suspected lesion and mail it to a laboratory.[1]

To fail to do a dark-field examination on a suspected chancre is criminal carelessness.

Directions for obtaining serum for examination are taken verbatim from Supplement No. 6 to Venereal Disease Information, published by the United States Public Health Service:

> If the lesion is covered with a crust or scab, remove it. Then wash the lesion thoroughly with a gauze sponge wet with plain tap water (no soap) or with normal salt solution, to remove gross surface infection. This should be dried off, and the surface of the lesion abraded with a dry gauze sponge, sufficient to provoke slight bleeding and exudation of serum. As oozing occurs, gently wipe away the first few drops, especially if they contain much blood, waiting for a drop or two of clear serum to appear. Gentle squeezing is permissible. It is desirable to obtain serum from the depth, not the surface of the lesion. One or several drops of clear serum should be aspirated into a capillary tube (outfits supplied by many State health departments), the ends sealed with the wax compound supplied with the kit (not with heat), and mailed at once, special delivery (air mail if necessary), to the nearest health department laboratory, a telegraphic report being requested.
>
> If the dark-field from the surface of the sore is negative, or if the lesion is completely epithelized, one may aspirate the base of the lesion or a neighboring lymph node. For this is required a sterile record or tightly fitting Luer syringe fitted with a stout needle of at least 20 gage. A drop or two of sterile normal salt solution is drawn into the syringe. The overlying skin is painted with iodine and alcohol and the node (or indurated base of the lesion) steadied between thumb and finger of the left hand. The needle is inserted well into the node, penetration of the capsule being indicated by the ability to move the node with the needle. The drop of salt solution is injected into the body of the node, the needle is manipulated in various directions to macerate the tissue about its point, and the injected salt solution and tissue juice aspirated. A drop of this is placed on a clean slip and slide, and examined at once for *T. pallidum*, or aspirated into a capillary tube as described above and forwarded at once to the nearest laboratory.

The presence of *Treponema pallidum* in lymph from a suspected lesion makes a positive diagnosis of syphilis. Failure to find the organism does not mean that the lesion is not syphilitic, and dark-field examinations should be made on at least 5 consecutive days before the search is abandoned. During this time local applications and antisyphilitic treatment should not be used. If the dark-field examinations are still negative the patient should be subjected to serologic follow-up for 4 months before the lesion is definitely considered nonsyphilitic.

Serologic Tests

In 1906 Wassermann, Neisser, and Bruck published their description of what is generally known as the Wassermann test, which was merely an extension of Bordet's complement fixation test. In 1922 there appeared the report of the first American flocculation test, that of Kahn (*73*). Since

[1] If the State health department laboratory is not prepared to do such tests the local medical societies should demand that it do so.

this time scores of other tests have been described, most of which have passed into the oblivion to which they were entitled.

At the time that this is written the following tests in America deserve special consideration:

1. Complement fixation tests, (*a*) Kolmer, (*b*) Eagle.
2. Flocculation tests, (*a*) Eagle, (*b*) Hinton, (*c*) Kahn, (*d*) Kline.

Of the flocculation tests, one of Eagle's tests and that of Kline are microscopic—these are known as microflocculation tests. Hinton and Davies also have a somewhat similar test. The ultra sensitive Kahn presumptive and Kline exclusion tests also deserve comment. Each year there appears a new test or two, most of which are without any great merit.

The latest available techic for these tests appears in Supplement No. 11 to Venereal Disease Information, published by the United States Public Health Service. Anyone who thinks he can obtain the latest from a textbook is unduly optimistic. At the rate that the serologists make improvements and changes, a technic is often out of date before the book is on the market.

The complement fixation tests have the great advantage of being easy to read, of being more readily adaptable for quantitative tests, and of being more satisfactory than flocculation tests for the examination of spinal fluid. They have the disadvantages of requiring a very careful technic, of requiring many reagents and of being expensive and slow to perform.

The flocculation tests are simpler, quicker, and easier to perform, but they require more care in reading.

The ultrasensitive tests give many false positive reactions in most hands although their originators seem to manipulate them satisfactorily. There would probably be few mourners if these tests were dropped entirely. A positive presumptive or exclusion test should never be accepted as establishing a diagnosis of syphilis without confirmation by at least two standard tests.

There is no "best test." Any of the modern tests are good if properly performed.

To be satisfactory a test must combine two factors: (1) It must be sufficiently sensitive to detect a very high percentage of the cases of syphilis, treated or untreated, and (2) it must have a very high specificity—giving positive reactions in syphilitic persons only. In order to furnish such results a laboratory must constantly check its results by (*a*) intralaboratory check, using two or more technics; (*b*) interlaboratory checks, in which one laboratory checks agaist another laboratory known to be reliable; and (*c*) most important of all, check serologic results against known clinical diagnoses in a good syphilis clinic. Unless these three checks are provided the laboratory is not satisfactory and should not be employed. Every physician should make it his duty to verify the use of these systems of checking in the laboratory of his choice.

The United States Public Health Service, through its Committee on Evaluation of Serologic Tests for Syphilis, has evaluated the various State

laboratories, (*74*, *75*, *76*, *77*, *77a*) and the State laboratories are supposed to evaluate the various county, municipal, hospital, and private laboratories within their own domains. Once this ideal is really enforced there will be better serum testing throughout the country.

Only three terms should be used in reporting results—positive, negative, and doubtful (indeterminate, repeat). To the clinician these terms have the following significance:

Positive.—Means syphilis, in the absence of yaws, leprosy, relapsing fever, infectious mononucleosis, active or very recently active malaria, and possibly at the time of menstruation in a few women and after the injection of large amounts of horse serum.

In the absence of a definite history or physical evidence of syphilis, a single unsupported serologic test from any laboratory should not be accepted as establishing a diagnosis of syphilis. In order to guard against possible technical or biologic false positives (less than 1 percent of the best available tests), the test must be repeated and the positive result confirmed in the same and, preferably also, in a different laboratory before the result can be accepted as sufficient evidence of syphilis. Occasionally, extended serologic study with a variety of different technics may be necessary to decide the validity of such a result.

Negative.—Although a positive test, properly controlled, means that the patient has syphilis, a negative test does not necessarily mean that he is free of it. The negative result is a priori presumption of the absence of syphilis, but it must be remembered (*a*) that no test so far developed is sufficiently sensitive to detect all cases of syphilis even if untreated and that from 5 to 10 percent of patients with actual syphilitic disease, especially late, will have negative blood tests; (*b*) that the test may be negative as a result of previous antisyphilitic treatment; or (*c*) that in the first 10 to 14 days after the appearance of a primary lesion the test is usually negative, the diagnosis hinging on dark-field examination or serologic follow-up. Among the commonest errors of medical practice are the treatment of primary syphilis as chancroid, cutaneous gumma as cancer or tuberculosis, syphilitic osteomyelitis as of pyogenic or tuberculous origin, and tabes dorsalis as "neuritis" because the serologic test was negative.

Doubtful.—This result cannot be interpreted without full clinical data, and from the serologic standpoint signifies only an unsatisfactory test which should be repeated. It may mean syphilis, e. g., in the primary stage before the test has become completely positive, or in any stage as a result of reduction in the strength of the test by means of treatment. On the other hand, it may mean technical error or a biologically false reaction. Unless syphilis is definitely known to exist clinically, a doubtful result cannot be interpreted without further serologic study, and the report should therefore be qualified by the laboratory with the words "Indeterminate. Repeat!"

When a laboratory employs several tests it should report each one separately. In a certain percentage of instances the results will not agree

for even a relatively insensitive test will occasionally detect a positive reaction that a more sensitive test misses. Also a complement fixation test will sometimes detect a reaction missed by the flocculation tests. The converse is occasionally true. But once again let it be emphasized that a diagnosis must never be made on one lone result. This should always be confirmed.

The results given by the good tests are as follows:

1. In primary syphilis 70 percent positive. It is usually believed that the test becomes postive between the tenth and fifteenth day.
2. In untreated secondary syphilis the tests are positive in over 99.5 percent of all instances.
3. In untreated late syphilis the tests are positive in over 90 percent of all instances.
4. In treated late syphilis the tests are positive in from 50 to 90 percent of all instances, depending on the amount of treatment.
5. In congenital syphilis, the tests are almost always positive in the early cases and usually positive in late cases.

The "follow-up Wassermann" is what the name implies, the use of a serologic test twice a week for 5 weeks and monthly thereafter to the expiration of 4 months in cases of suspected chancre when the dark field is negative. Calculate the time periods from the first appearance of the lesion.

The "provocative Wassermann" theoretically depends on one or more injections of arsphenamine causing a negative serologic reaction to become positive. This test is of doubtful value. At present the tendency is to administer two or three injections of arsphenamine and then to test the blood two or three times a week for some 5 weeks.

The quantitative tests are of less value in diagnosis than in following the effects of treatment. There is a totally false assumption on the part of many physicians that the plus-minus, single plus, two plus, three plus and four plus system of reporting is quantitative. As a matter of fact this scheme of reporting covers only about 1 percent of the field of positive results. When tests are reported in this way the plus-minus, single plus, and two plus reports should be interpreted as doubtful, and the three and and four plus as positive.

Quantitative tests are of particular value in following the course of the so-called "Wassermann-fast" patients. They are also of great value in spinal fluid examinations as well as in all patients in whom the serologic response seems rather slow. In other words they are of much more value in following the course of the treated patient than in diagnosis alone.

It goes without saying that all donors for blood transfusion should have a test done immediately before the blood is drawn, and they should be examined for history or physical signs of syphilis—especially chancres—even though the blood test is negative.

Roentgen-ray examination of the aorta and of the bones is of great value. No patient should ever be discharged from treatment without such an examination of the aorta. A thorough skeletal raying will sometimes show evidences of bone syphilis; in late syphilis it is sometimes a diagnostic aid of great importance. The changes in the epiphyseal line may be of some value in the diagnosis of congenital syphilis. Unerupted Hutchinson's teeth can often be detected. Examination of the viscera is often unsatisfactory.

It is now recognized that syphilis is a frequent cause of aortitis, and that this lesion may result in either a dilated aorta or in aneurysm. Aneurysm of the thoracic aorta is comparatively easy to recognize by almost any type of roentgen-ray examination, while that of the abdominal aorta is frequently difficult to diagnose because of the liver shadow. Padget and Moore (*78*) have recently decided:

"From examination of the evidence it seems clear that teleroentgenography in the postero-anterior position offers no reliable aid toward the early diagnosis of uncomplicated syphilitic aortitis, and the usefulness of other methods of examination is far from established. The studies of various workers, particularly Fray, regarding the use of the left anterior oblique position for teleroentgenography, preceded and supplemented by fluoroscopy, seem the most promising and should be further elaborated, and the roentgenologic findings should be closely compared with clinical and necropsy data. The preferable method of investigation would be by serial roentgenographic studies of groups of normal and diseased individuals, at periodic intervals over a lifetime, ending with necropsy confirmation of the presence or absence of aortic disease."

Syphilitic lesions of the lungs cannot always be recognized by radiologists. The lesions are most apt to be in the lower lobes, but tuberculosis may give a similar picture. The shadows are not supposed to bear a distinct relation to the bronchi. Other conditions that may cause trouble in differential diagnosis are carcinoma, pneumoconiosis, and unresolved pneumonia.

Syphilitic ulcers of the stomach cannot always be told from peptic ulcers or cancer. Diffuse syphilitic infiltration cannot be distinguished from fibrosis due to other causes. These, however, are rare conditions. Unless a surgical emergency exists the therapeutic test should be used if syphilis is suspected.

Syphilitic periostitis may show as a flat plaque or as a periosteal tumor associated with other bone changes. In mild cases it can be confused with the results of trauma, in advanced cases with tuberculosis and sarcoma.

The osteochondritis of congenital syphilis can apparently be simulated by rickets and perchance by other bone conditions due to disturbed nutrition.

Summary of Diagnostic Knowledge

I. Triumphs of laboratory diagnosis

A. Chancre:
   1. Dark field positive in 90 percent of cases during first 2 weeks.
   2. Blood reaction positive in 90 percent of cases during second 2-week period.
   3. Follow-up Wassermann is 99 percent decisive.

B. Secondary syphilis:
   1. Blood reaction positive in 99.8 percent of all cases, in good laboratories.

C. Late syphilis:
   1. Blood reaction positive in at least 90 percent of untreated cases.
   2. Blood reaction positive in 75 percent of moderately treated cases.
   3. Spinal fluid examinations decisive in 90 percent of cases of neurosyphilis.
   4. Roentgen-ray examinations decisive in aneurysm of aorta, and in 95 percent of osseous syphilis.

D. Congenital syphilis:
   1. Blood reaction positive or becomes positive within first 2 years of life in 99 percent of all cases.
   2. Dark-field examination of umbilical vein positive in a high (undetermined) percentage of cases.

II. Laboratory limitations in diagnosis

A. Chancre:
   1. Dark field positive in only 90 percent of early cases.
   2. Dark field positive in a lower percentage of cases as chancre becomes older.
   3. Dark field unreliable in mouth lesions.
   4. Dark field frequently negative if local treatment has been given chancre.
   5. Gland puncture only 60 percent positive.
   6. Blood serologically negative for the first 10 to 14 days.
   7. Total positive blood serologic findings during chancre stage only 70 percent.

B. Secondary manifestations:
   1. Dark field unreliable in mouth lesions.
   2. Blood serum reaction negative in 0.3 percent due to zonal reactions.

C. Late lesions:
   1. Dark field of no value.
   2. Blood serum reaction negative in 5 to 10 percent of all instances.

3. Spinal fluid examinations negative in 10 percent of all cases of neurosyphilis, this with marked disagreement among individual serologists. Examination frequently negative in meningovascular syphilis and tabes.
4. False positive reactions are given in many cases of leprosy, yaws, relapsing fever, active or very recently active malaria, and infectious mononucleosis, and not too infrequently in menstruating women and after the injection of horse serum.
5. Roentgen-ray examinations for aortic, pulmonary, and abdominal syphilis are sometimes unreliable.

D. Congenital:

1. False positive reactions are given during first 2 to 6 weeks from toxemia.
2. Cord-blood examinations are unreliable.
3. Roentgen-ray examinations of long bones are sometimes unreliable unless expertly interpreted.

To recapitulate briefly, the diagnosis of chancre is a laboratory procedure; every genital sore should be suspected of being syphilitic until proven otherwise. The dark-field examination of the initial lesion and, if this is negative, gland puncture should always be employed. After the tenth day the blood serologic reaction is usually positive. In doubtful cases the Wassermann follow-up should always be used. The therapeutic test is mentioned only to be condemned; nonsyphilitic lesions often heal spontaneously.

In secondary syphilis, the blood serum is positive in well over 99 percent of all instances.

Latent syphilis, in the absence of a definite history, can be diagnosed only by positive serum reactions.

Late syphilis, if untreated, gives positive serologic findings in at least 90 percent of all instances. A thorough physical examination including roentgenograms and examination of the spinal fluid should disclose an additional 5 percent.

If the spinal fluid is examined, at least 95 percent of all cases of neurosyphilis can be recognized.

Congenital syphilis can be recognized early by examination of the umbilical vein wall for spirochetes, and later by serologic tests in at least 99 percent of all cases.

Part IV

Treatment

General Considerations

Treatment is a means of rendering the patient noninfectious and often of assuring a permanent cure as well as of relieving his symptoms.

The following points may be emphasized:

1. Treatment of early syphilis must be continuous with at least one injection per week, and courses of arsenicals should be alternated with courses of bismuth or mercury. With late syphilis this is desirable but not so essential.

2. No matter what the serologic tests show a certain minimal amount of treatment must be administered.

3. A simple rule with reference to early syphilis is that treatment should usually be given continuously until 1 year after the patient's blood becomes and remains negative. In late syphilis (acquired or congenital) reversal of the blood reaction is not a good guide for the termination of treatment.

4. The amount per dose of arsphenamine or of one of the heavy metals should be related to the patient's weight; a 90-pound woman and a 250-pound man should certainly not be given the same dosage.

5. The physician should take all responsibility for treatment, and the patient should be encouraged to report his complaints.

6. A weekly record of the weight of the patient should be kept to see how he is standing treatment.

7. The urine should be examined for albumin and casts every 2 weeks, especially when bismuth or mercury is being administered.

8. The hemoglobin should be estimated at least once a month, especially in women.

9. In case of sore throat or ulcers in the mouth or pharynx during arsenical therapy obtain a white count and differential.

10. The mouth should be examined at each visit when mercury or arsphenamine is being given.

11. Watch the sclerae for jaundice.

12. Before administering arsphenamine, the trunk and anticubital areas should be inspected to make certain there is no arsphenamine rash. Inquire whether there has been itching or burning of the skin. Look also for petechiae and purpuric spots.

13. Watch for peripheral neuritis.

14. Blood pressure should be taken weekly, especially in pregnancy.

15. Any source of focal infection should be removed as soon as the patient is rendered noninfectious; the kidneys and liver have a sufficient toxic load to bear from therapy without the extra load absorbed from an infectious process.

16. The diet should be nutritious and full.

17. Alcohol should be dispensed with; sprees are of no aid to the syphilitic patient—remember what they do to a tuberculous patient.

18. Always have the spinal fluid examined, not later than after the third course of arsphenamine in early syphilis and much earlier in late syphilis.

19. Treat the patient on the basis of a yearly contract; do not stop treatment when his cash fails. If necessary refer him to treatment at government expense rather than release him to the community partially treated or untreated.

20. If in doubt obtain consultation.

21. Cases of late syphilis in elderly persons, if asymptomatic, are often best left untreated or given mild therapy such as an occasional course of bismuth or "mixed treatment."

22. Warn infectious cases to avoid family and social contacts of a nature which may transmit the infection. Be specific and complete in such instructions.

23. Report each case to the health department, together with names and addresses of people from whom your patient may have acquired his disease and to whom he may have transmitted it.

Specific Therapy

A previous supplement (No. 6) to Venereal Disease Information (*79*) describes the technic of treating syphilis with the arsenicals and heavy metals in accordance with modern standards. [1] The general practitioner is referred to this handbook for guidance in all phases of routine treatment of early, latent, and late syphilis, syphilis in the pregnant woman, and other phases of systematic treatment not dealt with in the present work. Supplement No. 6 may be obtained from the Superintendent of Documents, Washington, D. C., price 10 cents.

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[1] Referring to the "Preparation and Technic of Administration of Arsphenam nes" in Supplement No. 6, p. 27, it should be noted that old arsphenamine can be dissolved in sterile distilled water and that alkalinization can safely be done in a much simpler manner than is directed in that publication. Correct alkalinization is important; many deaths have been due to the injection of acid mixtures. Some years ago it was taught that the disodium salt of arsphenamine was the proper one to inject and that an extra 25 percent of alkali must be added to produce this. However, it was soon learned that this produced many cases of phlebitis. At the present time, we simply wait until the arsphenamine dissolves, then add 10 percent sodium hydroxide until the early precipitate disappears, and test by pouring a drop on a bit of red litmus paper to make sure of alkalinity.

After the administration of bismuth it is good practice to urge the patient to take a short walk following an intramuscular injection. This really provides automassage.

In addition to the use of drugs in the treatment of syphilis a number of other measures may also be employed. The best known of these are (*a*) malarial therapy, (*b*) typhoid vaccine intravenously, and (*c*) "artificial" heat therapy.

Malarial therapy is given by inoculating the patient with malaria. In this country the inoculation is usually performed by transfer of blood with a syringe rather than using mosquitoes as intermediate hosts. It has been found that many Negroes are immune to infection with the tertian strain, but that the quartan strain is satisfactory. It is generally agreed that the estivo-autumnal strain should never be employed as it is too dangerous. From 1 to 5 cc. of blood from a patient with malaria is given intravenously to the syphilitic patient under treatment. Injections are as successful with apyrexial as pyrexial donors. The average incubation period is 3 to 8 days with tertian malaria but longer with quartan malaria. The recipient should always be hospitalized, and the treatment should never be administered to one who has heart, kidney, or lung disease of a serious nature or signs of increased intracranial pressure.

From 8 to 15 malarial paroxysms are permitted and then quinine is administered. Should the diastolic blood pressure fall below 70 or should tachycardia (pulse rate of 120 or over) persist during the afebrile period, quinine should be given. After the cessation of treatment there should be a complete rest period of at least 1 week. Care should be taken that the patient is well of the malaria before he is discharged.

The mortality from malarial injections is approximately 1 percent in carefully selected patients.

Malarial therapy is the treatment of choice in paresis, tabes, optic atropy, malignant syphilis (which is rare) and interstitial keratitis (if it is resistant to chemotherapy). Second courses are rarely indicated.

Typhoid-paratyphoid therapy has a distinct field of usefulness as a second course of fever therapy in malignant syphilis and when malaria is not available. The commercial typhoid-paratyphoid vaccine is employed intravenously, the initial dose being approximately 50 million. For the first 5 injections the dose is doubled each time unless contraindications appear. Some 12 injections should be given at approximately 4-day intervals. Both dosage and interval depend on the amount of reaction from the previous injection. If the temperature fails to reach 102° F. the injection should not be counted. Frequently there is nausea and occasionally vomiting within 20 minutes after the injection.

"Artificial" heat therapy is induced in various ways—by hot baths, hot blankets, diathermy, and by a special hypertherm cabinet of which the Kettering machine is probably the best. Any form of heat therapy should be administered only by one who has had special training, for a number of deaths have been reported. The patients must be carefully selected and well looked after while undergoing treatment, which is a matter of

hours. The apparatus is usually expensive, and the results not superior to malarial therapy.

The Swift-Ellis treatment is a special procedure whereby an arsphenamine or arsphenaminized serum is injected into the subarachnoid space. It is dangerous except in the hands of an expert. It is used now mainly for primary optic atrophy and the lightning pains of tabes.

Treatment of Syphilis Complicated by Other Diseases

Syphilis is a frequent and long-lasting disease; naturally there may be other complicating conditions.

One is old age, that is over 60. If the syphilis is latent, it is often best left untreated or given mild treatment such as occasional courses of bismuth or "mixed treatment," especially if there are any other constitutional disturbances. Prolonged, punishing treatment usually is not indicated save in syphilis of the cardiovascular or nervous system.

Malignancy is not an absolute contraindication for antisyphilitic treatment. Eash case must be judged on its merits.

Tuberculosis of the lungs is not made worse by arsphenamine or bismuth, but the iodides and fever therapy should not be employed. Tuberculosis of the adrenals is a contraindication to arsphenamine.

Pneumonia in the presence of syphilis is sometimes complicated by delayed resolution. If the patient is syphilitic, antisyphilitic medication may be of distinct aid.

Diabetes, if controllable, is not a contraindication to the treatment of syphilis.

Nephritis means that mercury should never be used and bismuth should be employed sparingly and cautiously.

Arteriosclerosis, essential hypertension, and rheumatic heart disease are not contraindications to antisyphilitic treatment so long as compensation is adequate. Again each case should be judged on its individual merits.

Allergic diseases are not a contraindication to treatment for syphilis.

Arthritis likewise is not a contraindication.

Prognosis

The outlook in syphilis depends upon many things: (1) Severity of the infection; (2) immune processes of the individual; (3) race; (4) sex; (5) pregnancy; (6) complicating diseases; (7) treatment; and (8) special types of infection.

1. Some infections seem more severe than others; whether or not there are different strains of spirochetes is still a moot question.

2. The nature of immune processes is still unknown. Certain it is that there are many spontaneous recoveries; even a neurosyphilis may "burn out" leaving only a few scars in its wake, as evidenced by permanently changed reflexes.

3. The Negro is less liable to neurosyphilis but more liable to cardiovascular syphilis. Various studies show that his life expectancy is shortened more than is that of the white.

4. Women are less liable to severe types of infection than are men; this is true of all races and is not necessarily from the benefits conferred by pregnancy. As has already been stated Negro women seldom suffer from paresis or tabes.

5. Pregnancy has a beneficial effect on the disease. Syphilis, however, has a deleterious effect on pregnancy.

6. Complicating diseases may be serious, independently, or they may interfere with treatment.

7. Continuous treatment, of sufficient amount, given early in the course of the disease is the best preventive for later trouble.

8. The probability of symptomatic and serologic "cure" with *adequate* treatment in various types of the disease is well expressed in the following table modified from Moore's textbook.

The probability of symptomatic, and serologic "cure" in various types of early and late syphilis (modified from Moore) [1]

Type of syphilis		Probability, expressed in approximate percent, if adequate treatment is given, of—	
		Symptomatic "cure"	Serologic "cure"
Early	Seronegative I	100	100
	Seropositive I	92–98	85–95
	Early II	92–98	85–95
	Recurrent II	70–80	70–80
Latent	Early	92–98	80–90
	Late	90–95	3–035
Benign late	Skin or mucosac	90–95	30–40
	Bones and joints	80–90	10–25
	Other organs	60–80	30–40
Cardiovascular	Simple aortitis	70–80	30–40
	Aortic insufficiency	0	30–40
	Aneurysm	0	30–40
Central nervous system	Early	60–70	85–95
	Diffuse late	40–60	30–40
	Tabes	20–35	60–70
	Paresis	15–30	0–10
Congenita [1]	Early	40–60	40–60
	Late	0–80	10–20

[1] From Dr. J. E. Moore's book, "The Modern Treatment of Syphilis." Courtesy of Charles C. Thomas, publisher, Springfield, Ill.

For many years there have been clinicians who felt that the natural resistance of the individual patient was even more important than treatment. Many cases of spontaneous cure have been reported from time to time. The figures given by Bruusgaard (*80*) are both important and much quoted.

Boeck, who was chief of the syphilis clinic in Oslo between the years 1891 and 1910, gave only tonic treatment to cases of primary and secondary syphilis, or but a minute amount of mercury or potassium iodide in special cases. During these two decades 2,181 patients were treated. Between 1925 and 1927 Bruusgaard followed up these individuals. He was successful in reexamining 309 of the original number, and in determining the cause of death in another 164, on 40 of whom autopsies were secured. All the living patients submitted to thorough physical examination and had blood Wassermann tests, although spinal fluid examination was rarely done. The conclusions were that neurosyphilis developed in 9.5 percent of all patients, and that cardiovascular syphilis developed in 12.8 percent. In a total of 23.1 percent of these patients a serious, often fatal late lesion of syphilis developed, and in an additional 12.2 percent late lesions of the skin, mucous membranes, or bones developed. A total of 64.6 percent of the total number passed through the whole period of observation without being seriously inconvenienced, and 27.9 percent of spontaneous cures was the apparent result.

These figures would indicate that out of every 100 patients acquiring syphilis 23 would develop late lesions which would either kill or incapacitate; 12 would develop a milder type of late lesions; and 64 would pass through life unharmed.

This work of Bruusgaard emphasizes the need for treatment of patients with syphilis, but it also encourages the physician with a certain healthy optimism as to ultimate prognosis.

Part V

Prophylaxis

Status of Prophylactics and Recommended Technics

"The prevention of syphilis and gonorrhea by chemical or mechanical means is supplementary to and not a substitute for the prophylaxis of these diseases by educational measures which employ ethical and religious motives. Nor does chemical or mechanical prophylaxis justify any relaxation of efforts to reduce to a minimum exposure to infection by discouragement of prostitution and other forms of sexual promiscuity."

This is the view (*81*) of a special joint committee appointed by the American Social Hygiene Association and the United States Public Health Service to review the history and status of venereal disease prophylactics and to make recommendations on their place in syphilis control.

In the case of syphilis and gonorrhea, as with other communicable diseases, the Committee's report continues, the best and surest method of prevention of infection is the avoidance of exposure. Educational, religious, sociologic, and legal activities which tend to prevent exposure to infection are of great importance. At the same time, however, the Committee is fully aware of the fact that sexual promiscuity is a very important factor in their spread. To decrease the number of carriers among this group of men and women, chemical and mechanical prophylaxis is necessary and hence is complementary to educational measures.

The place of chemical and mechanical preventive measures is at the point where educational, religious, social, and legal efforts have failed to prevent exposure to infection. At that point preventive medicine offers reasonably efficient methods of prevention, which, if correctly applied, will in the majority of instances prevent the exposed person from becoming infected and from becoming a possible source of infection to those with whom he may later have contact. Thus not only one individual but that individual's family and community may be relieved of the burdens—medical, social, and economic—of syphilis and gonorrhea. The employment of chemical and mechanical prophylaxis will preserve the efficiency of men required for defense or service of the Nation in time of peace or of war. This being the case, it becomes the moral obligation of sanitarians to urge the wide dissemination of all available knowledge regarding such procedures.

After carefully reviewing the available scientific data as to the efficiency of various means of chemical and mechanical prophylaxis, the Committee makes the following specific recommendations:

The chemical and mechanical prevention of syphilis and gonorrhea.[1]

1. Safest method—
   - A. Use a condom of standard type.
   - B. Thoroughly wash the genitals and adjacent parts with soap and water as soon as possible (the sooner the better, but within 1 hour at most) after removal of the condom.

[1] The directions for the prevention of syphilis and gonorrhea apply to the prevention of all other venereal diseases as well.

2. In the absence of a condom—

   A. Thoroughly wash with soap and hot water as already described.

   B. After urination, inject 6 cc. of 2 percent strong protein silver solution, or other efficient, nonirritating germicidal solution into the urethra and hold for 5 minutes.

   C. Rub 33 percent ointment of mild mercurous chloride (calomel ointment) into the genitals and adjacent parts.

The habit of cleanliness materially reduces the risk of infection. For the proper application of 2B and C, skilled attention and use of a syringe are necessary. Prophylactic treatment of this type can be given by physicians, by some clinics, and in prophylactic stations where they exist.

The Committee emphasizes the fact that the foregoing suggested preventive measures are not 100 percent successful. Their efficacy depends first on the reliability of the materials used. A defective condom does not give the same degree of protection as a sound article. The strong protein silver solution or the mild mercurous chloride may not be of the proper strength or may be inactive. Second, washing and application of chemicals may be delayed too long after exposure. Drunkenness may prevent correct application of any of these methods. It may be stated, however, that when these methods are followed correctly they will in the majority of instances prevent infection with syphilis or gonorrhea.

The medical profession and public health agencies, both official and voluntary, bear a heavy responsibility in the matter of the prevention of syphilis and gonorrhea by chemical and mechanical means. Since these methods are efficacious they would, if widely understood and correctly utilized by those who expose themselves to the danger of infection, result in a great diminution of syphilis and gonorrhea and would thereby greatly reduce personal, family, and community disasters and the economic losses that result from these infections.

Comments [2]

It seems clear, therefore, that health education with regard to syphilis and gonorrhea should include simple, frank, and explicit directions as to chemical and mechanical prophylaxis. This information should be included in its proper setting and in appropriate language.

It seems apparent also that, in addition to instructing the public regarding this preventive medical method, civilian, military and naval, medical and health authorities have the obligation to provide the facilities through which chemical and mechanical prophylaxis may be made available when and where needed. The authorities also have the responsibility for preventing the commission of fraud through the sale of worthless products to the public for the prevention of these diseases.

Finally the Committee is impressed with the fact that there are many unsolved and administrative problems within the scope of chemical and mechanical prophylaxis and the provision of adequate facilities for these procedures. It is considered that research in this field should be continued.

A fuller discussion of the chemical, chemotherapeutic, and mechanical technics of prophylaxis may be found in Supplement No. 6 to Venereal Disease Information (*78*).

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[2] In this initial report the Committee has purposely avoided going into detail, believing that only general principles should be discussed. In the full report detailed methods will be given at length.

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ADDENDUM

Implications From the Viewpoint of the Negro Physician

By

The Commission on the Eradication of Syphilis of the National Medical Association

D. W. Byrd, M. D., *Chairman*, Norfolk, Va.
E. D. Burke, M. D., *Secretary*, Norfolk, Va.
J. G. Gathings, M. D., Houston, Tex.
Oma H. Price, M. D., New York City, N. Y.
G. L. A. Pogue, M. D., Bedford, Va.
O. D. Chambers, M. D., Nashville, Tenn.
E. W. Weaver, M. D., Rome, Ga.
Harold H. Whitted, M. D., Montgomery, Ala.
Roscoe C. Giles, M. D., Chicago, Ill.
William M. Thorne, M. D., Charleston, S. C.
N. L. Barnett, M. D., Belzoni, Miss.
John E. Eve, M. D., Hot Springs, Ark.

With the collaboration of

George William Bowles, M. D., *Ex-President*, National Medical Association.
A. W. Dumas, Sr., M. D., *Ex-President*, National Medical Association.
A. N. Vaughn, M. D., *President*, National Medical Association.
H. E. Lee, M. D., *President-elect*, National Medical Association.

The important role of the National Medical Association in the fight against syphilis was recognized by Surgeon General Thomas Parran in his book, Shadow on the Land. Said he:

> The first national organization formally to vote cooperation with the syphilis control campaign of the United States Public Health Service was the National Medical Association composed of Negro physicians. This association at its meeting in Philadelphia in the summer of 1936 appointed a Commission on Eradication of Syphilis, which came to Washington in September to present a tentative program and ask how their cooperation could be made most effective. They offered unremitting efforts to enlist the services of all colored physicians, pharmacists, dentists, nurses, social workers, and affiliated organizations, a number aggregating more than 15,000.

The Commission for the Eradication of Syphilis has sought through the Negro clergy, race newspapers, instructors in colleges and public schools, parents, and through fellow members of the medical profession to educate the 15,000,000 individuals in its racial group to protect themselves against syphilis. Racial consideration is only important in finding the causes and

means of prevention of the high rate of Negro infection. Beyond that point, antisyphilis education means education for all people, and it is to this end the Commission has directed its efforts.

In another direction, the Commission has worked for the establishment of clinics for Negroes manned by Negro physicians, nurses, and social workers. Our experience in Norfolk, Va., during the World War has been used as a guide to success in this effort. Norfolk was a great mobilization center for overseas transportation, and the Federal government made great effort to protect these men from venereal disease during their stay in Norfolk.

At this time a Negro community center was established by the city of Norfolk. The center included a venereal disease clinic under Negro personnel and management. The interest of this clinic was directed toward protecting both the sailors and soldiers and the civilian population. The efficiency and conscientiousness of the clinic's staff in this work was attested by City Manager Ashburner and Health Commissioner Schneck.

The experience gained by these Negro physicians, nurses, and social workers led to the establishment in 1932 of the Norfolk public clinic with Negro personnel and management. It now serves an urban, rural, and transient colored population of more than 100,000.

A recent report by Dr. E. D. Burke, secretary of the Commission, shows that the clinics in which Negroes are treating their own people are increasing in number and in efficiency. Colored physicians in urban and rural districts of the South are organizing small laboratories and clinics so that the colored population may have easily accessible facilities for diagnosis and treatment. The State of North Carolina has taken the lead in this activity. Unfortunately, while the number of Negro clinics is increasing, they as yet represent but a fraction of the number needed, particularly in the deep South.

To achieve the ultimate value of this work, the training of Negro physicians in venereal disease control must be extended and Negroes qualified in medicine and public health be given places in the State and local health agencies.

FIGURE 1.

Treponema pallidum as seen by dark-field microscope.

FIGURE 2.

A chancre in one of its commonest locations, the corona. In this instance the lesion is very indurated and shows no ulceration, a true Hunterian chancre.

FIGURE 3.

Typical ulcerated chancre of the labia majora. (From the collection of Dr. Harry M. Robinson.)

FIGURE 4.

Typical chancre of the lower lip. Note enlarged lymph nodes in right side of neck. Extragenital lesions are very rare in the Negro.

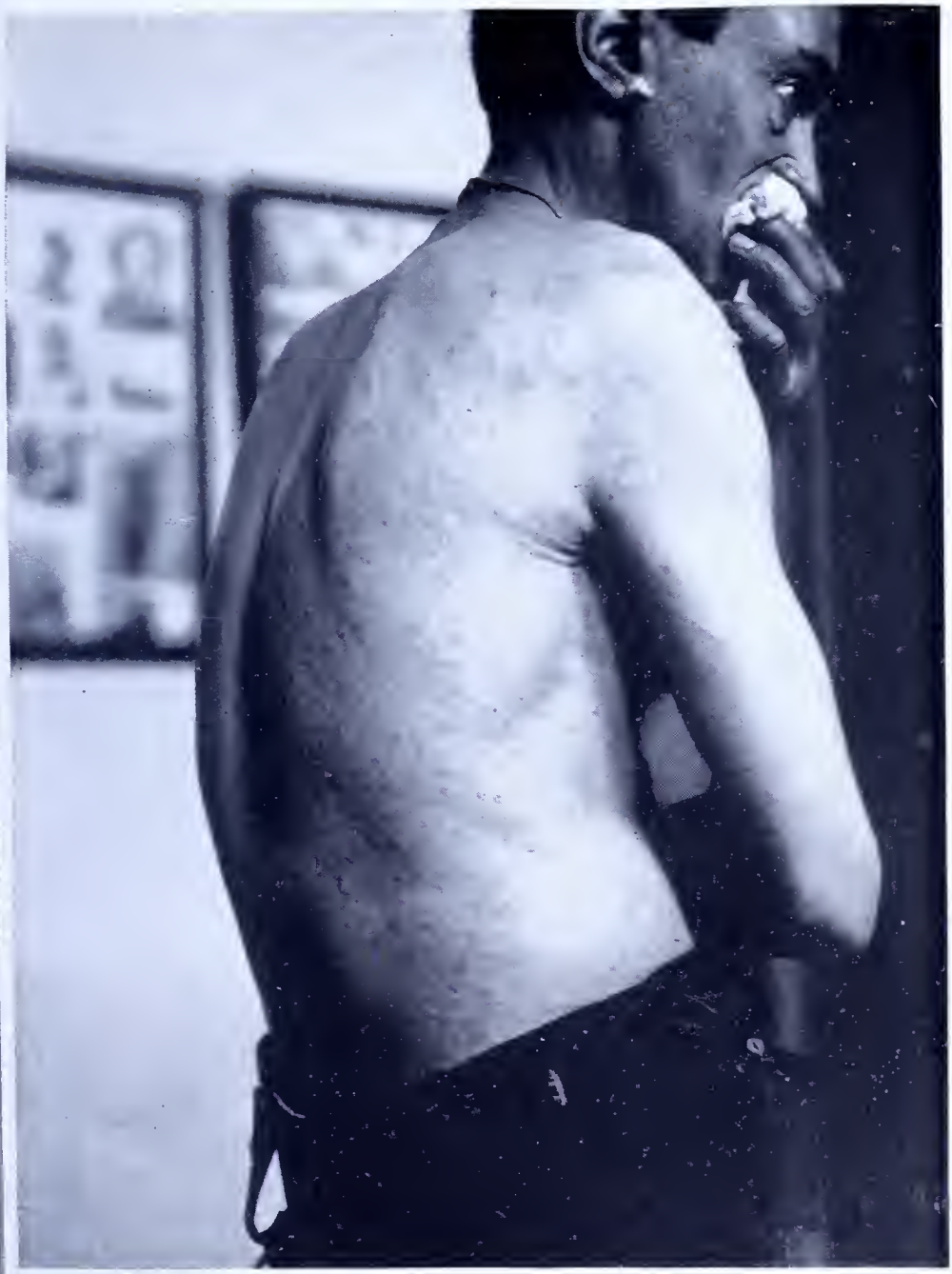

FIGURE 5.
Maculopapular syphilis which resembles hives.

FIGURE 6.
Miliary or follicular papular syphilis.

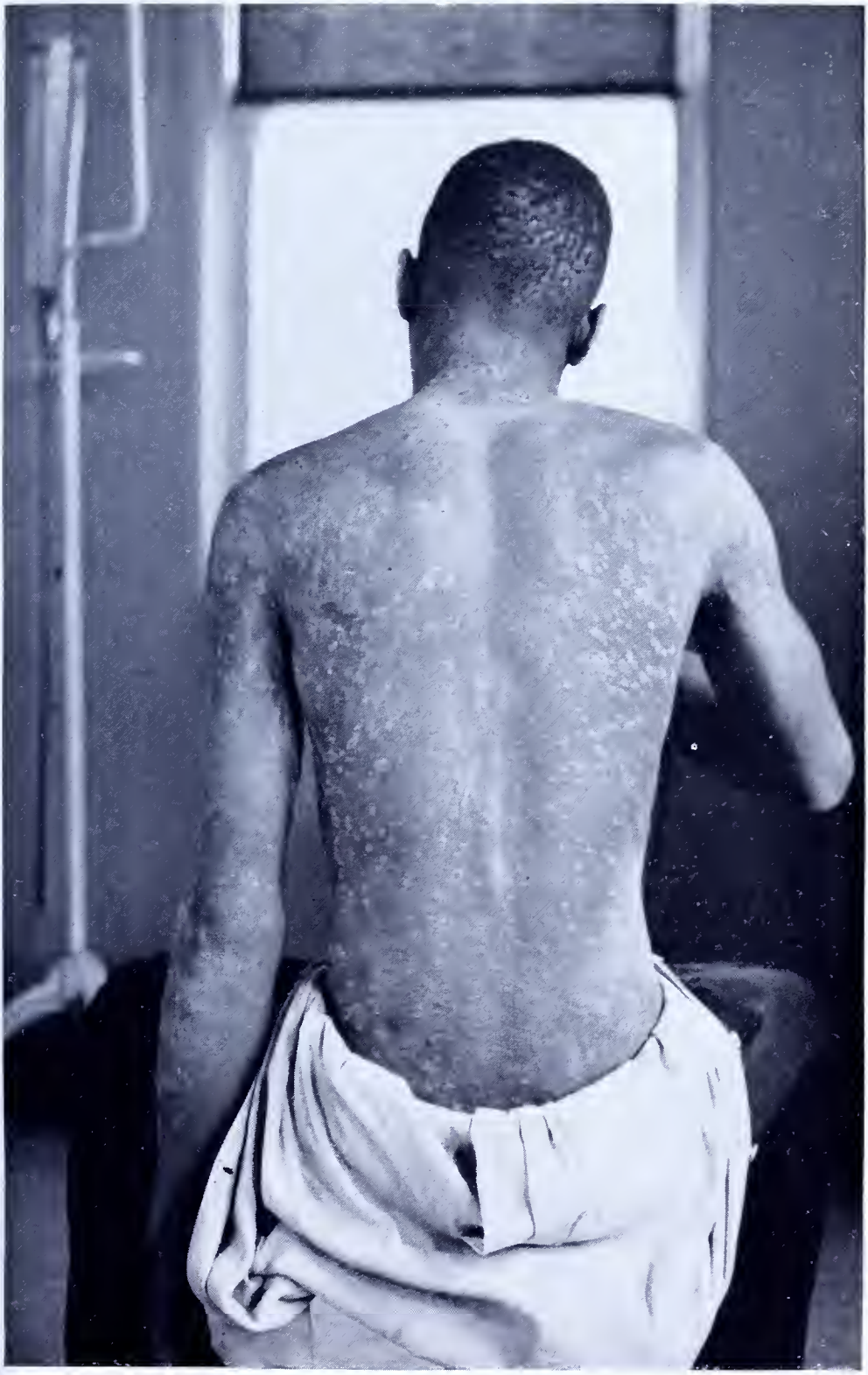

FIGURE 7.
Flat papular syphilis, with a moderate syphilitic alopecia.

FIGURE 8.

Papular syphilis with large semiglobular lesions.

FIGURE 9.
Typical annular syphilitic lesions in a usual situation.

FIGURE 10.

Condylomata are especially frequent in Negro women. The lesions are highly contagious. (From the collection of Dr. H. M. Robinson.)

FIGURE 11.

Serpiginous nodular late syphilis. Notice scar tissue in center of lesions.

FIGURE 12.

Ulcerative gummatous lesions of syphilis.

FIGURE 13.

Hutchinson's teeth. Only the second set are affected.

FIGURE 14.
Saber shins of congenital syphilis.

The Treatment of Syphilis

WITH

ARTIFICIAL FEVER COMBINED WITH CHEMOTHERAPY

RESULTS OF TEN YEARS OF EXPERIENCE

A Critical Review

By

- WALTER M. SIMPSON, M.D., F.A.C.P.

  Director, Kettering Institute for Medical Research, Miami Valley Hospital, Dayton, Ohio; Special Consultant, Division of Venereal Diseases, U. S. Public Health Service; Commander, Medical Corps, U. S. Naval Reserve

- H. WORLEY KENDELL, M.D.

  Associate Director, Kettering Institute for Medical Research, Miami Valley Hospital, Dayton, Ohio

- DONALD L. ROSE, M.D.

  Research Associate, Kettering Institute for Medical Research, Miami Valley Hospital, Dayton, Ohio

SUPPLEMENT NO. 16 TO VENEREAL DISEASE INFORMATION

FEDERAL SECURITY AGENCY

PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

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EUROSYPHILIS

N THE BASIS of the experiences of many reliable investigators during
e past decade it can now be stated that artificial-fever therapy [1] of neuro-
hilis is at least as effective as malarial therapy. The past 5 years have
tnessed a notable decline in the hyperenthusiastic and sometimes extrava-
nt claims made by certain advocates of one or the other method. Out
the controversy has emerged a more rational clarification of the relative
erits of the two procedures. Several authoritative communications have
ntributed greatly to this wholesome situation.

APPRAISAL OF MALARIAL THERAPY AND ARTIFICIAL-FEVER THERAPY

By Wagner-Jauregg

The brilliant analysis, The Present Management of Progressive Paralysis
Julius Wagner-Jauregg, published in 1939 (*1*), a short time before his
ath, is a masterpiece of unprejudiced objectivity. After examining
tically the results obtained with malarial therapy and with artificial-
er therapy, Wagner-Jauregg, the father of malarial therapy, made these
nificant statements:

The method of treatment by elevation of body temperature to the height of fever by
ysical means has been used in a large number of diseases and in many has been shown
be effective. Insofar as used in progressive paralysis, this method concurs with malarial
rapy. . . . Results showed that after treatment with physically induced fever,
tients with paralysis exhibited the same remissions as those treated with malaria.
ny of the authors who carried out the treatment of paralysis with physically induced
er reported that the number of remissions obtained was as great or greater than with
larial therapy and that the number of improvements was equally good.

Furthermore, it is a well-known advantage of artificial fever that one can regulate the
ght of the temperature reached, the length of the single fever periods, and the dura-
n of fever-free rest periods according to the condition of the patient. Moreover, in
rying out the treatment, hospitalization is not necessary. The last consideration is
ecially important in case one is dealing not with clear-cut progressive paralysis, but
her with its prophylaxis, that is with a positive spinal fluid in the latent stage. These
tients as a rule are still working, and malarial treatment would require several weeks
interruption of their work. Finally, if by means of artificial fever and subsequent
motherapy, the goal of treatment is not reached, namely, the production of negative
nal fluid, then one still has time to utilize malarial treatments. . . .

Since, as a rule, one can determine as early as a few weeks after the completion of

[1] The term "artificial-fever therapy" denotes the production of fever by physical
ans.

fever treatment, whether a full remission can be expected to occur, it is recommend that the course of fever therapy be immediately repeated in prognostically unfavorab cases. It is expedient in cases in which it is possible to do so, to change the type of fev treatment, namely to follow a course of malarial therapy with a course of artificial fev and vice versa.

Much too little use is made of the scheme of dividing the course of malarial thera into two parts, according to which after three or at most four attacks of fever the malar is controlled by quinine. Then after an interval, during which specific treatment given, a new malarial inoculation is made, which, due to the fact that the patient h recovered in the interval, can be tolerated better and for a longer period than the fi half of the course. . . . Such a divided course can be carried out even more easi with artificial fever.

In case experience should confirm, on the basis of a large amount of material, th malaria and artificial fever combined with intensive treatment with pentavalent arsenica in the treatment of progressive paralysis result in the same number of equally comple and lasting remissions, then still other nonmedical considerations would decide t choice of the method.

One must also consider the question from an economic standpoint. So far as t fever-producing agent is concerned, malarial treatment has an unquestioned advantag The few cubic centimeters of blood contributed by a febrile paretic to the patient to l treated costs nothing, and in case it has to be sent elsewhere for inoculation, the expen is negligible. Furthermore, several patients can undergo a course of malarial thera in the same room under the supervision of a single trained person.

The apparatus necessary for the production of artificial fever is costly. . . . Duri the course of a treatment the uninterrupted presence of a person trained in the compl technic of the apparatus is necessary; also, only as many cases can be treated simu taneously as there is available equipment.

. . . Many have emphasized as an advantage of artificial fever therapy its lack danger as compared with the danger of malarial therapy (fatalities). Occasional deat from treatment with artificial fever have, however, been reported. Deaths report following malarial therapy do not represent uniform material. In regard to progressi paralysis, there are patients who die even without any treatment. One can attribu only those deaths to malarial therapy which occur during malarial treatment or at mo one month thereafter and of those only the patients who died after the technic of malari therapy (diminishing the fever by means of small doses of quinine, dividing the cour of treatment into two parts, careful observation of heart action and blood pressure, etc had been sufficiently developed. Without careful adherence to proper technic treatme with artificial fever also would result in more deaths.

REPORT OF THE COMMITTEE ON NONSPECIFIC THERAPY OF SYPHILIS

United States Public Health Service

In August 1936, about 3 years before Wagner-Jauregg's classic repo appeared, Surgeon General Thomas Parran of the United States Publi Health Service appointed a subcommittee[2] of the Cooperative Clinica

[2] This committee was composed of Paul A. O'Leary, M. D. (chairman), Mayo Clini Rochester, Minn.; Walter L. Bruetsch, M. D., Central State Hospital, Indianapoli Franklin G. Ebaugh, M. D., Colorado Psychopathic Hospital, Denver; Harry C. Sol mon, M. D., Boston Psychopathic Hospital; Stafford L. Warren, M. D., Strong Mem rial Hospital, Rochester, N. Y.; and Walter M. Simpson, M. D., Miami Valley Hospita

oup to study and evaluate the various forms of nonspecific therapy used the treatment of neurosyphilis. In addition to submitting to the Public alth Service for statistical analysis clinical records from all of the institu-ns represented by the members of the committee, the clinic directors [3] five hospitals offered for analysis the records of their institutions.

t required nearly 4 years to collect the data and to subject it to rigid alysis by disinterested professional statisticians. The report of the com-ttee, Malaria and Artificial Fever in the Treatment of Paresis, appeared August 1940 (*2*). The study was designed to compare the therapeutic ults obtained by the use of artificial fever produced by physical methods th those obtained by the use of inoculated malaria in the treatment of resis (dementia paralytica). The results were evaluated in terms of both nical and serologic responses observed after the independent use of either thod of fever therapy, with or without the associated employment of emotherapy.

Only unequivocally paretic patients who had been observed for more than years following the commencement of fever therapy were considered. he records of 1,420 such patients were pooled for statistical study. Of ese, 1,100 patients were treated with malaria and 320 with artificial fever. All were classified by the degree of syphilitic meningo-encephalitic involve-nt when fever therapy was begun. Patients with "mild paresis" were atively free from signs of deterioration, and their mental symptoms were ually transitory. Those classified as having "intermediate paresis" hibited symptoms of manic excitement, depression, or other psychiatric ndromes in addition to evidence of moderate deterioration. The third ssification, that of "severe paresis," included those who gave evidence of vanced deterioration.

The clinical results of therapy were defined as (a) "remission," in which ere was sufficient clinical recovery to permit the patient to return to his mer socio-economic status; (b) "improved," which denoted complete or rtial disappearance of clinical manifestations without corresponding im-ovement in the capacity to return to the former socio-economic status;) "unimproved," in which there was no detectable clinical evidence of ange in the course of the disease; (d) "progressed," which indicated that e clinical status was less satisfactory after treatment than before; and

yton, Ohio. All had had extensive experience with either malarial therapy or with ificial-fever therapy or with both. Assistant Surg. Gen. R. A. Vonderlehr, Chief of Division of Venereal Diseases, U. S. Public Health Service, was also a member of the mmittee and was assisted by Lida J. Usilton, M. A., I. V. Sollins, Ph. D., A. P. Iskrant, A., and other members of the Statistical Section of the Division of Venereal Diseases. A. E. Bennett, M. D., Bishop Clarkson Memorial Hospital, Omaha; Harold N. Cole, eveland City and University Hospitals, Western Reserve University; J. R. Blalock, D., and Leland E. Hinsie, M. D., New York State Psychiatric Institute and Hospital, w York City; Frank R. Menagh, M. D., Henry Ford Hospital, Detroit; and Captain nest H. Parsons, M. C., U. S. Army, Fitzsimons General Hospital, Denver.

(e) "death," which included deaths during therapy, or deaths regardless of cause occurring within 3 months subsequent to therapy.

The yearly clinical remission rates per 100 patients treated were based upon the method of therapy and upon the degree of paretic involvement when fever therapy was begun. Thus, the total successful results of therapy were determined at the conclusion of any given year within the entire period of treatment and posttherapy observation. The increase in the percentage of successful outcomes of therapy within a given year could thus be obtained by subtraction (table 1).

TABLE 1.—*Average Yearly Clinical Remission Rates (Cumulated)*

[Committee on Nonspecific Therapy of Syphilis, U. S. Public Health Service]

THREE-YEAR TREATMENT-OBSERVATION

End of each year of treatment-observation	Rate of remission per 100 paretics under treatment-observation							
	Mild		Intermediate		Severe		Total	
	Malaria	Artificial fever	Malaria	Artificial fever	Malaria	Artificial fever	Malaria	Artificial fever
1	36.4	37.7	13.7	16.2	0.0	3.9	13.8	18.0
2	45.1	48.4	20.2	21.0	.5	9.0	18.9	24.7
3	51.7	50.2	24.2	23.6	.9	11.3	22.4	27.2
FOUR-YEAR TREATMENT-OBSERVATION								
1	36.4	35.2	13.3	16.8	0.0	2.9	13.4	16.9
2	44.7	45.9	19.6	19.2	.5	8.6	18.4	22.6
3	51.9	47.3	23.5	22.0	1.0	11.3	21.9	25.1
4	52.3	52.8	25.1	30.9	1.0	11.3	22.8	30.3

As regards the patients with mild or intermediate paresis there were no statistically significant differences between the rates of remission obtained with malarial therapy and those obtained with artificial-fever therapy. In other words, equally good clinical results were obtained following either method of fever therapy in patients with mild or intermediate paresis. Sharp and statistically reliable differences were noted, however, between the results of the two methods of therapy among patients suffering from severe paresis at the beginning of fever therapy; here there was distinct superiority of remission rates following artificial-fever therapy, as noted in table 1.

The clinical responses were best when fever therapy was instituted early in the course of the disease. Thus, at the end of 3 or 4 years of treatment-observation, more than one-half of the patients with mild paresis treated

with either method of therapy had clinical remissions. Similarly, with either method of fever therapy, the rates for clinical recovery were reduced to approximately one in four patients with intermediate paresis. While the proportion of remissions was distinctly less in patients with severe paresis, 11 percent of patients with severe paresis obtained clinical remission after artificial-fever therapy, while only 1 percent had clinical remission following malarial therapy.

For purposes of this study, treatment-deaths were defined as deaths occurring not only during the course of fever therapy but also during the succeeding 3 months regardless of cause. Utilizing such criteria, the total crude death rate was higher with malaria (13 percent) than with artificial fever (8 percent). The frequency of death was greatest among the patients with severe paresis (25.8 percent of malaria-treated cases and 17.9 percent of those treated with artificial fever). By contrast, among patients with mild paresis there were no deaths during the course of artificial-fever therapy and four deaths during malarial therapy; 2.3 percent of the patients with mild paresis treated by either method died within 3 months. Among those with intermediate paresis, 9.4 percent of the malaria-treated patients and 6.5 percent of those treated with artificial fever died during treatment or within 3 months following treatment. Thus, while these individual differences are not statistically significant, they all point in the same direction, indicating that the percentage of deaths under malarial therapy was higher than with artificial-fever therapy within each degree of paretic involvement.

An analysis of the relative speed with which remissions were attained revealed that approximately 90 percent of the successful results occurred by the end of the third year by either method. In mild paresis remissions were obtained from 1 to 2 years earlier than in intermediate or severe paresis.

If clinical improvement was delayed beyond the second year following fever therapy by either method, remission did not occur. Thus, the more prompt the clinical response, the better was the prospect for eventual remission. Once clinical remission was obtained, the chances of its being maintained were 95 out of 100. There was no statistically valid difference in the relapse rates following either method of fever therapy.

In determining the relation of clinical to serologic results, it was found that clinical success was not accompanied by complete serologic reversal (of blood and of spinal fluid) in more than one-half of the cases. Thus, emphasis is again given to the fact that successful clinical outcome is not necessarily dependent upon serologic response.

Regardless of the method of therapy, the percentages of serologic reversal rates of both blood and spinal fluid increased as the duration of the treatment-observation period grew longer. Positive blood reactions reversed more rapidly though not in greater proportion than positive spinal fluid reactions. The percentage of blood reversals was greater in the malaria-

treated group, but reversal occurred more rapidly in those treated with artificial fever.

The necessity for employing auxiliary chemotherapy with either method of fever therapy was indicated by both the significantly higher proportion of spinal fluid reversals and by the maintenance of such reversals in patients receiving concomitant or subsequent chemotherapy or both. In patients treated with fever plus chemotherapy the annual rates of reversal of spinal fluid reactions from positive to negative as well as the rates of blood reversal were higher with malaria than with artificial fever, but this difference was assumed to be due to the greater amount of chemotherapy (17 percent more) administered to the malaria-treated patients. Without the use of auxiliary chemotherapy there were no differences between the spinal fluid and blood reversal rates of patients treated with malaria and those treated with artificial fever. The reversal rates of blood and spinal fluid were approximately twice as great with as without the use of auxiliary chemotherapy. Among patients not receiving auxiliary chemotherapy 42 percent of all spinal fluid reversals subsequently relapsed, as contrasted with 24 percent spinal fluid relapses among patients treated with auxiliary chemotherapy.

In three-fourths of the cases in which both clinical and serologic recovery were reported, clinical remission either preceded serologic reversal or occurred during the same year. When clinical remission preceded serologic reversal, the average difference in time was between 2 and 3 years.

A correlation of the clinical outcome with the duration and the intensity of fever, measured by rectal temperature levels, left no doubt that there was a definite correlation between the height and duration of fever and the clinical results. The highest percentage of clinical remissions was obtained in the two groups of patients who experienced either an average of 69 hours of fever above 101° F. (38.3° C.),[4] of which 70 percent was at a level above 105° F. (40.6° C.) with a maximum temperature of 106.9° F. (41.6° C.); or in those who received an average of 44 hours of fever above 101° F. (38.3° C.) of which total time 57 percent was above 106° F. (41° C.) with a maximum temperature of 107° F. (41.7° C.). On the other hand, the clinical results were distinctly inferior, to the point of being practically nil, in those patients who received an average total of 30½ hours above 101° F. (38.3° C.), with an average of 12.8 sessions of 2½ hours comprising the total course, with a maximum temperature of 104.9° F. (40.5° C.), and with an average of 26 percent of the total fever time at a level between 104° and 104.9° F. (40° to 40.5° C.). A careful analysis of the data revealed that no clinical advantages were gained by submitting patients to rectal temperatures above 106.5° F. (41.4° C.). The committee was

[4] Throughout this report all statements regarding body temperature refer to rectal temperature levels, usually obtained by constantly indicating or recording electrical thermometers in cases in which artificial-fever therapy was employed.

unanimous in its belief that temperatures between 106.5° and 106.7° F. (41.4° and 41.5° C.) are apparently the highest rectal temperature levels which can be used with safety in clinical practice and then only when surrounded by adequate safeguards. Experience has taught that the administration of fever therapy at levels above 106.7° F. (41.5° C.) introduces unnecessary hazards.

REPORT BY EWALT AND EBAUGH, UNIVERSITY OF COLORADO

Treatment of Alternate Patients With Artificial Fever or Malaria

In his classic appraisal of the relative advantages of artificial fever and malarial therapy, Wagner-Jauregg (*1*) directed particular attention to a preliminary report (*3*) by Barnacle, Ebaugh, and Ewalt, of the University of Colorado Psychopathic Hospital in 1936, of a comparative study of artificial-fever therapy combined with and followed by tryparsamide, and of malarial therapy followed by tryparsamide. Wagner-Jauregg pointed out that the procedure adopted by Barnacle, Ebaugh, and Ewalt for an equalized investigation of fever therapy by the Kettering hypertherm and by inoculation with malaria was superior to that employed in other studies of this kind.

The Denver investigators, who had had long experience with malarial therapy, decided to employ the "alternate case" method of determining the comparative usefulness of artificial-fever therapy and of malarial therapy. Strict alternation was practiced in assigning successive patients to one or the other therapeutic program. The same criteria as those adopted by the Committee on Nonspecific Therapy of the United States Public Health Service (of which Professor Ebaugh is a member) were used in classifying paretic patients as "mild," "intermediate," or "severe." Thus, the advantages were had of unity of material, time, place, and observers.

In the preliminary report (1936) of the therapeutic results accruing from this controlled study of 60 patients during a 1-year period, it was stated that in the artificial fever-chemotherapy group (30 patients) there was remission in 12 (40 percent), as compared with remission in 7 (23.3 percent) of the 30 malaria-chemotherapy patients. Nine (30 percent) of the patients treated with artificial fever-chemotherapy were improved, while 12 (40 percent) of the malaria-chemotherapy patients responded likewise. Thus, of those treated with artificial fever, 21 (70 percent) were benefited, as compared with a similarly favorable outcome in 19 (63.3 percent) of the malaria-treated patients. No patients died during the course of artificial fever, while one patient died of cerebral hemorrhage 2 weeks after the apparently successful conclusion of the course of fever treatments. One patient died during malarial therapy and 3 malaria-treated patients died during the year following treatment.

Here again it was found that the highest proportion of remissions occurred among patients with "mild" paresis. Improvement in the serum reactions of the spinal fluid was comparable in both groups and there was no parallelism between clinical and serologic improvement.

In a current report (*4*), Ewalt and Ebaugh provide additional information regarding the progress of the original groups of patients and submit data on a 5-year comparative study of artificial-fever therapy and malarial therapy, based upon the assignment of 232 patients with dementia paralytica either to artificial-fever therapy or to therapeutic malaria. The authors were encouraged to continue the comparative study of alternate paretic patients because of the favorable results obtained with artificial-fever therapy in the original series, and to determine if possible why "for reasons not entirely clear to the authors, certain clinics treating neurosyphilis have been skeptical of the therapeutic value of artificial fever in this neuropsychiatric disorder."

TABLE 2.—*Dementia paralytica: Types of treatment and clinical results during 5-year period*

[Ewalt and Ebaugh, University of Colorado Psychopathic Hospital, Denver, Colo.]

Clinical status	Artificial fever		Therapeutic malaria	
	Number of cases	Percentage	Number of cases	Percentage
		Percent		*Percent*
Remission	25	19	7	7
Improved	68	50	50	51
(Remission and improved)	(93)	(69)	(57)	(58)
Unimproved	31	22	27	27
Died within 3 months of treatment	2	1.4	5	5
Died subsequently	8	6.6	9	9
Total	134	99.0	98	99

As the work at the Colorado Psychopathic Hospital progressed, it became apparent that certain paretic patients who were not considered to be candidates for malarial therapy because of such concomitant disorders as cerebral arteriosclerosis, chronic nephritis, or diabetes could tolerate artificial-fever therapy if due caution was exercised. Hence, the only deviation from the "alternate-patient" plan in the more recent study was to include 37 such patients in the group treated with artificial fever and auxiliary chemotherapy. Thus, the totals are brought to 134 patients treated with artificial-fever therapy and to 98 patients treated with malaria.

The comparable character of the two groups as regards the type of fever therapy administered to patients in the different clinical categories is

shown by the fact that 44 (32 percent) of the patients treated with artificial fever and 31 (31 percent) of the malaria-treated patients were classed as "severe," while 70 (52 percent) of those treated with artificial fever and 55 (55 percent) of those treated with malaria were classified clinically as "intermediate." The average age of patients treated with artificial fever was 40 years, and the average age of those treated with malaria was 42.6 years. The duration of symptoms prior to the institution of fever therapy was 22.8 months in the artificial-fever therapy group and 17.2 months in the therapeutic-malaria group.

During the first 3 years of this investigation the patients treated with artificial fever received 50 hours of fever at a rectal temperature of 105° to 106° F. (40.6° to 41.1° C.), given as 10 treatment sessions of 5 hours each. In the last 2 years of the study it was found that a series of 12 individual fever sessions of 3 hours each (a total of 36 hours of fever) at a rectal temperature of 105.8° F. (41° C.) was equally effective and had the decided advantage of permitting the treatment of a greater number of patients.

The extraordinary success of the Colorado investigators in following the progress of these patients is indicated by the fact that, with the exception of those who died, all of the malaria-treated cases and two-thirds of those treated with artificial fever during the preliminary study (reported in 1936) were followed during the entire 5-year period. Most of those who disappeared were known to have responded favorably to fever-chemotherapy. The employment of skilled social workers, utilizing a rotating roster, was of great value in inducing patients to return for progress studies at intervals of 6 months following the completion of the course of chemotherapy subsequent to fever therapy.

The clinical therapeutic results achieved by the Colorado workers are summarized in table 2. Of the 134 paretic patients receiving artificial-fever therapy, 25 (19 percent) achieved remission, as compared with 7 (7 percent) of the 98 patients treated with malaria. Sixty-eight (50 percent) of those treated with artificial fever and 50 (51 percent) of the patients receiving therapeutic malaria were improved. The criteria used in determining "remission" and "improvement" were the same as those adopted by the Committee on Nonspecific Therapy of Syphilis of the United States Public Health Service.

Thus, 69 percent of the patients treated with artificial fever were benefited, as compared with 58 percent of the malaria-treated patients. It is interesting to observe that approximately the same differences existed in the 5-year series as in the 1-year series described in the preliminary report by the same investigators. While the improvement rate and the relapse rate during the periods of posttherapy observation were approximately the same in the 1-year and 5-year studies, the differences appeared to be due to the better immediate response of patients treated with artificial fever. The authors express the belief that this difference may be due to the fact that

with artificial fever the patients may be treated at higher temperature levels than is possible with malarial therapy. Another factor to which significance was attributed is that patients usually gained weight during the course of artificial-fever therapy and in most instances were in distinctly better physical condition at the conclusion of the course. The patients treated with malaria, on the other hand, usually lost weight and developed varying degrees of anemia despite energetic efforts to prevent these sequelae.

The results obtained with either form of fever therapy, grouped according to the degree of severity of the paretic symptoms, are presented in table 3. As in the cooperative study made by the United States Public Health Service, the therapeutic results were best in "mild" paresis—45 percent of remissions with artificial fever and 25 percent with malarial therapy. Among those with "intermediate" symptoms and signs, 23 percent obtained remission following artificial-fever therapy as compared with 7 percent of those who received therapeutic malaria. Full remission did not occur in any patient with "severe" paresis following either method of fever therapy. The proportions of "improved" patients were essentially the same with either mode of therapy, except that among the patients with "severe" paresis, 41 percent responded favorably to artificial-fever therapy as compared with 29 percent of those receiving therapeutic malaria. Of the patients with "mild" paresis, all were benefited by artificial-fever therapy, and only one failed to respond favorably to malarial therapy.

TABLE 3.—*Dementia paralytica: Classification of clinical groups in relation to clinical results*

[Ewalt and Ebaugh, University of Colorado Psychopathic Hospital, Denver, Colo.]

Clinical status	Artificial fever						Therapeutic malaria					
	Mild		Intermediate		Severe		Mild		Intermediate		Severe	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Remission	9	45	16	23	0	0	3	25	4	7	0	0
Improvement	11	55	39	54	18	41	6	50	35	64	9	29
Unimproved	0	0	12	17	19	43	1	8	11	20	15	48
Died	0	0	3	4	7	16	2	17	5	9	7	23
Total	20	100	70	98	44	100	12	100	55	100	31	100

None of those treated with artificial fever died during the course of fever therapy, while two died during malarial therapy. Two patients (1.4 percent) treated with artificial fever died within 3 months of treatment, as compared with five deaths (5 percent) during this interval among those treated with malaria. The number of subsequent deaths was not signifi-

cantly different—8 patients (6.6 percent) in the artificial fever group and 9 patients (9 percent) in the therapeutic malaria group.

While marked clinical improvement was maintained in many individuals with persistently positive serum reactions in the spinal fluid, there was an appreciably greater proportion of serologic reversals from positive to negative among those who experienced clinical remission or improvement. The spinal fluid serologic reactions were reversed to negative in 11 percent of those treated with artificial fever and in 6.1 percent of those receiving therapeutic malaria. The reactions became less positive in 35 percent of those in the artificial-fever therapy group and in 28.5 percent of the malaria-treated patients. The serologic reactions remained positive in 35 percent of those treated with artificial fever and in 40.8 percent of those who received malarial therapy. Eighteen percent of the patients who were treated with artificial fever and 24.4 percent of those who were treated with malaria were not available for final evaluation of cerebrospinal fluid reactions. A large proportion of those who failed to return regularly for reexamination were known to have achieved a successful clinical result. Thus, of the 109 patients treated with artificial fever who were available for repeated serologic reexaminations, 62 (57 percent) exhibited reversal or improvement in their serologic status; of the 74 malaria-treated patients subjected to adequate serologic study, 34 (46 percent) showed similar degrees of serologic improvement.

Ewalt and Ebaugh found that intensive chemotherapy subsequent to fever therapy is an essential requirement for sustained optimum results. These authors expressed the belief that the variations in therapeutic results reported from different clinics may well be due in large part to the degree of effort exerted in inducing patients to return at regular intervals for chemotherapy and for clinical and serologic reexaminations.

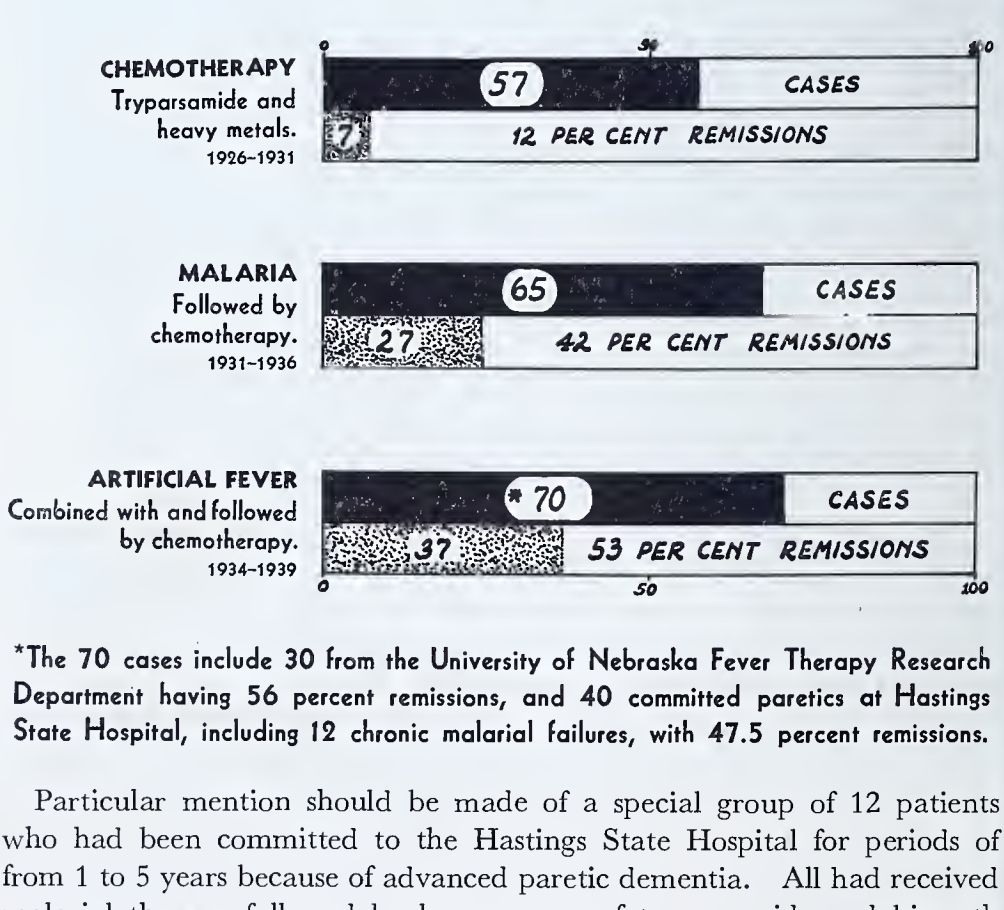
Finally, it is pertinent to observe that Ebaugh and Ewalt have now abandoned malarial therapy in favor of artificial-fever therapy.

RECENT REPORTS BY BENNETT AND COWORKERS, UNIVERSITY OF NEBRASKA, OMAHA

The favorable experiences of Prof. A. E. Bennett and his associates at the University of Nebraska (Omaha), with artificial-fever therapy combined with chemotherapy in the management of the various stages of neurosyphilis have been described in five recent publications (*5*). One report (*5c*) deals with a review of a 5-year experience in the treatment of dementia paralytica by this combined method at the University of Nebraska College of Medicine and at the Hastings (Nebraska) State Hospital. The apparatus employed for the production of fever was the Kettering hypertherm. Comparisons were made of the artificial fever-chemotherapy method with previous experiences in the use of chemotherapy alone (tryparsamide plus heavy metals) and in the employment of malaria inoculation followed by

chemotherapy. The comparative incidence of remissions resulting from the use of these therapeutic programs is shown graphically in chart 1. It may be observed that the percentage of paretic patients achieving remission with artificial fever combined with and followed by chemotherapy (53 percent) was significantly greater than that which followed either malaria inoculation and subsequent chemotherapy (42 percent) or chemotherapy alone (12 percent). The patients treated with artificial fever received 50 hours of fever (rectal temperature) above 105° F. (40.6° C.), induced by means of the Kettering hypertherm, usually given in 10 to 15 3- to 5-hour sessions. Chemotherapy during and subsequent to the fever sessions consisted of injections of 0.06 gm. of mapharsen (meta-amino-parahydroxyphenylarsine oxide), usually preceded by concurrent injections of a bismuth salt (0.01 gm.). The malaria-treated patients were allowed to have 12 chills which were followed by tryparsamide and bismuth therapy, usually for several years. Those paretic patients who were treated with chemotherapy alone received adequate courses of tryparsamide and heavy metals (bismuth and mercury).

CHART I



*The 70 cases include 30 from the University of Nebraska Fever Therapy Research Department having 56 percent remissions, and 40 committed paretics at Hastings State Hospital, including 12 chronic malarial failures, with 47.5 percent remissions.

Particular mention should be made of a special group of 12 patients who had been committed to the Hastings State Hospital for periods of from 1 to 5 years because of advanced paretic dementia. All had received malarial therapy followed by long courses of tryparsamide and bismuth

therapy. None achieved complete remission. The patients in this refractory group were given a course of 50 hours of artificial fever combined with auxiliary mapharsen therapy. Four (33 percent) of those patients obtained complete remission, 3 (25 percent) were improved, while the remaining 5 patients were unaffected. Thus, 58 percent of those classed as malaria-failures were benefited by subsequent artificial-fever therapy.

In addition to the 37 (53 percent) of the 70 patients treated with artificial fever combined with mapharsen who exhibited remissions, there were 20 additional patients (28 percent) who were improved. Thus, 81 percent of the patients responded favorably. The spinal fluid serologic reactions were reversed to negative in 24 patients (34 percent), and became less positive in 26 (37 percent).

Bennett and his associates (*5a, b, e*) have reported similarly favorable experiences in the treatment of asymptomatic neurosyphilis, tabes dorsalis, the tabetic form of dementia paralytica, and meningovascular neurosyphilis with combined artificial fever and chemotherapy. Of 8 patients with asymptomatic neurosyphilis, all of whom had had long-continued chemotherapy previously, the spinal fluid serologic reactions were reversed to negative in 5 patients, were less positive at the time of the last observation in 2, and were unchanged in one uncooperative patient who had only 29 hours of fever.

All of the 12 patients with meningovascular neurosyphilis, of whom 8 had not responded to presumably adequate chemotherapy, were benefited. Four patients had hemiparetic features; 3 had palsies of the cranial nerves; 3 had aphasic, convulsive and confusional psychotic reactions; 3 had chronic headaches associated with increased intracranial pressure and meningitic phenomena; and one had a syndrome simulating multiple sclerosis. Except for one patient with hemiplegia and another with occasional convulsions, all were rid of their symptoms. Prompt and striking improvement was observed in the aphasic and meningitic symptoms. Because of the presence of vascular complications, many of these patients would have been unable to tolerate malarial therapy. The great advantage in controlling by physical means the height and the duration of the fever was particularly apparent in this group of patients.

In 25 patients with tabes dorsalis, the predominant symptoms were lightning pains and gastric crises in 17 patients, ataxia in 7 patients, and "cord bladder" in 2 patients. The clinical results included complete relief from symptoms in 18 patients (chiefly those with root pains), some degree of improvement in 5, and no improvement in 2. One patient experienced recurrence of root pains; in another the disease progressed to dementia paralytica after a long period of apparent improvement.

As a result of these and other studies, the authors drew the following conclusions. Patients of advanced years or in poor physical condition, including those with such complications as hypertension or aortitis, can be

treated with greater safety with artificial fever because the height and duration of fever can be controlled readily. The concurrent employment of artificial fever and chemotherapy increases the therapeutic effectiveness of both. The prescribed number of hours of fever is more easily obtained by physical methods. The results of treatment are definitely correlated with the height and duration of fever. Continuous hospitalization is not a requirement when artificial-fever therapy is used except for those exhibiting severe psychotic manifestations. The relapse rate is lower with physically induced fever. The mortality rate is less with artificial fever. A significant proportion of neurosyphilitic patients who fail to respond to malarial therapy or who obtain only moderate degrees of improvement following such treatment are benefited by subsequent artificial-fever therapy. Certain patients who would not be accepted as candidates for malarial therapy may be benefited by judiciously applied artificial-fever therapy. Artificial-fever therapy combined with chemotherapy is the most effective method of therapy now available for resistant asymptomatic neurosyphilis and for all forms of symptomatic neurosyphilis.

Artificial fever therapy has replaced malarial therapy in public and private institutions in Nebraska.

REPORT BY BROMBERG, WASHINGTON UNIVERSITY, ST. LOUIS

Bromberg (*6*) has recently described his successful experiences in the treatment of various manifestations of neurosyphilis with artificial-fever therapy (utilizing the Kettering hypertherm) combined with chemotherapy, during a 3-year period. The therapeutic program employed by Bromberg was essentially similar to that used by Bennett and his coworkers and by Ewalt and Ebaugh.

It is of more than passing interest to observe that Bromberg and his skilled associates have treated over 300 patients with artificial-fever therapy, many of whom were quite ill, without a single fatality.

Of 76 patients treated by Bromberg for various manifestations of neurosyphilis, there were 21 with dementia paralytica, 14 with the tabetic form of dementia paralytica (taboparesis), 21 with tabes dorsalis, 8 with meningovascular neurosyphilis, and 12 with asymptomatic neurosyphilis. Eighteen of the 21 paretic patients (86 percent) were improved; 3 were not benefited. Of the 14 patients with the tabetic form of dementia paralytica, 12 (85 percent) were classified as improved. Among the 21 patients with tabes dorsalis, 18 (86 percent) responded favorably; relief of root pains and gain in weight were outstanding features of the clinical response of the tabetic patients. All of the 8 patients with meningovascular neurosyphilis experienced prompt and marked improvement. The spinal fluid serologic responses were uniformly good in all of the 12 patients treated for asymptomatic neurosyphilis.

REPORTS BY TRAUTMAN, U. S. MARINE HOSPITAL, NEW ORLEANS

In comprehensive reviews of the experiences in artificial-fever therapy during the past 6 years at the United States Marine Hospital, New Orleans, Trautman (7) tells of the treatment of 985 patients (a total of 5,500 treatment-sessions), with one death. One hundred and nine patients were treated for neurosyphilis. The apparatus employed was the Kettering hypertherm. Most of the patients had received routine chemotherapy in the Marine Hospital or elsewhere, with little or no benefit, prior to the institution of artificial-fever therapy. Chemotherapy was employed by Trautman in conjunction with the fever sessions and was continued after the course of fever treatments was terminated.

Most of the patients admitted to the United States Marine Hospitals are officers and sailors of the merchant marine. Since these men receive free medical care from the United States Public Health Service, they must agree to remain under observation at the discretion of the medical officers. Thus, there is provided an exceptional opportunity to study the results of treatment under the more favorable circumstance of continuous hospitalization than is usually possible in general hospitals The only disadvantage is that it is sometimes difficult to obtain data on the progress of such patients some years after the course of treatment. In a high proportion of cases, however, the patients have returned to the United States Marine Hospital at New Orleans or to some other United States Marine Hospital for such studies.

Fourteen patients with dementia paralytica received an average total of 60 hours of fever, at a rectal temperature level of 104°–105° F. (40°–40.6° C.). There were two patients who exhibited symptoms of "mild" paresis; one recovered completely; the other improved clinically but passed from observation. Of 8 patients with "intermediate" paresis, 6 obtained remissions and 2 were improved. There were 4 patients with "severe" paresis; one showed improvement, and in one the disease progressed; in the other 2, treatments were discontinued because of the severity of the disease and because of associated cardiovascular complications. Thus, of the 14 paretic patients, 10 (71 percent) are known to have been benefited, while the outcome is not known in one additional case.

Eleven patients with tabes dorsalis received an average of 13 fever treatment-sessions of 5 hours each, at a rectal temperature of 104°–106° F. (40°–41.1° C.), at intervals of 1 week. Of 5 patients with "mild" tabetic symptoms, 4 obtained complete symptomatic relief, and the fifth patient was markedly improved. In one case of "intermediate" tabetic involvement there was no improvement. The 5 patients with "severe" tabetic symptoms were benefited in that they were relieved of the associated pains. Hence, 10 (90 percent) of the 11 tabetic patients obtained some degree of clinical improvement. The spinal fluid serologic reactions were reversed to negative in 5 patients and became less positive in 2.

There were 13 patients with meningeal, vascular, or combined meningovascular neurosyphilis. Of the 7 patients with meningeal involvement, all responded favorably; prompt relief of symptoms was usually observed after the first fever session. Three of the four patients with vascular neurosyphilis had complete symptomatic recovery while the fourth had sufficient improvement to enable him to undertake light work. The 2 patients with meningovascular neurosyphilis were moderately improved. The spinal fluid reactions became negative in 7 of the 13 patients and were less positive at the time of last observation in 2; the serologic outcome in 2 patients is not known. The prompt disappearance of the meningitic symptoms and the restoration of the spinal fluid cell count and globulin content to normal levels were the outstanding features in this group. All were benefited by the treatment.

Seventy-one patients with asymtomatic neurosyphilis were treated by Trautman and his associates. Of the 45 patients in this group on whom adequate posttherapy observations were made, the spinal fluid serologic reactions were reversed to negative in 30 (66⅔ percent) while the remaining 15 retained some degree of serologic positivity. The blood serologic reactions became negative in 29. It is probable that the percentage of serologic reversals would have been greater if some of the patients had been observed over longer periods. None of the 45 patients, the outcome of whose treatment is known, has developed any evidence of clinical neurosyphilis.

RECENT REPORT BY NEYMANN, NORTHWESTERN UNIVERSITY, CHICAGO

To his many previous reports, Neymann (*8*) has contributed a recent summation of his experiences in the artificial-fever therapy of syphilis since his pioneering efforts in 1927. Neymann and his associates (Osborne, Koenig, Feinberg and Markson) have utilized electropyrexia (short-wave diathermy currents, now applied in an air-conditioned cabinet) combined with chemotherapy (tryparsamide plus bismuth or mercuty) in the treatment of 120 patients with dementia paralytica. Fifty-five (46 percent) achieved complete remission. In determining remission, Neymann included only those paretic patients who were not only rid of their symptoms, but who had also resumed their former or equivalent occupations and who had remained at work for at least 6 months. Twenty additional patients (17 percent) were improved. Thus, a total of 75 patients with dementia paralytica (63 percent) were benefited.

In a survey based upon the clinical results reported by some 50 investigators in the treatment with artificial fever produced by a variety of physical methods, of 975 patients with dementia paralytica, Neymann found that at least 266 (27 percent) had obtained remission, while 354 (36 percent) were improved. The recorded percentage of remissions is probably lower than the actual proportion, since Neymann included in this category only

those patients in whom there was unequivocal evidence of remission. In sum, 620 of the 975 paretic patients (63 percent) were benefited by artificial-fever therapy. In comparing these results with those attained with malarial therapy, Neymann stated that the use of artificial-fever therapy increased the total rate of improvement in patients with dementia paralytica by 21 percent and decreased the treatment-death rate to an almost negligible level.

In a similar analysis of the reported clinical results obtained by 17 investigators using several different physical modalities for the production of artificial fever in the management of tabes dorsalis, Neymann found that of 114 tabetics, 75 (66 percent) were improved. In his own series of 8 tabetics, all of whom improved, the disappearance of root pains was the outstanding feature of therapy. Tabetic crises and pains did not recur during periods of posttherapy observation extending from 1 to 3 or more years.

After 13 years of experience with artificial-fever therapy and after extensive previous experience with malarial therapy, Neymann has come to regard the "mythical, unproved and much extolled magical action of the plasmodium of malaria" in the treatment of neurosyphilis as a "fetish or taboo in the minds of its most ardent advocates."

REPORTS BY HINSIE AND BLALOCK, NEW YORK STATE PSYCHIATRIC INSTITUTE AND HOSPITAL, NEW YORK

In addition to providing further evidence of the merits of artificial-fever therapy, the reports by Hinsie and Blalock (*9*) are of particular significance in that a careful analysis was made of the results obtained with artificial-fever therapy alone, with artificial-fever therapy followed by a course of 12 or more injections of tryparsamide and bismuth, and with artificial-fever therapy combined with an injection of tryparsamide just prior to each fever treatment and followed by a course of tryparsamide after the conclusion of the course of combined fever-tryparsamide treatments. The apparatus employed by Hinsie and Blalock was the ultra high-frequency apparatus developed by Whitney, known as the "radiotherm." The data are based on a study of 146 adult patients with acquired dementia paralytica observed during a period of 5½ years. The patients in each group received 10 treatments at approximately 105° F. (40.6° C.), each of 7 hours' duration, on alternate days for the purpose of simulating the malarial character of the febrile course. At the end of the second year of posttherapy observation, the remission rate in the patients who received artificial-fever therapy alone was 18 percent; in those who received an equivalent amount of fever therapy followed by a course of tryparsamide therapy, the remission rate was 27

percent; in those receiving injections of tryparsamide in conjunction with and following fever therapy the remission rate was 30 percent. An additional 29 percent were improved following fever therapy alone, while the percentages of improvement in the other two groups were 36 and 35. On the basis of these and other studies, Hinsie and Blalock expressed the belief that the employment of fever therapy alone produces results comparable to those obtained with malarial therapy and that much more favorable results are obtained when chemotherapy is employed in conjunction with artificial-fever therapy.

In a recent communication (1938), Hinsie and Blalock have reported the serologic results of both blood and spinal fluid of patients treated for dementia paralytica with either malaria or artificial fever. The results are based on observations made in the same hospital during a 4-year period. At the end of the fourth year, the blood serologic reactions were reversed to negative in 28 percent of the malaria-treated patients and in 59.1 percent of the patients treated with artificial fever; the spinal fluid reactions became negative in 57.2 percent of those treated with malaria and in 63.6 percent of those treated with artificial fever. These workers also observed that, while serologic improvement is in general independent of the clinical response to either malaria or artificial fever during the first few years after therapy, a persistently positive serologic ensemble after the third or fourth year following fever therapy has considerable prognostic significance since it is much more frequently associated with an unfavorable clinical outcome.

In common with other investigators who have had extensive experience in the use of artificial-fever therapy, Hinsie and Blalock have found no evidence that the relapse rate of paretic patients is higher with artificial-fever therapy than with malarial therapy.

PERSONAL EXPERIENCES IN THE TREATMENT OF NEUROSYPHILIS

The history and progress of our work in artificial-fever therapy since its inception in 1931 has been recorded in several publications (*10*). Impressed by the successful clinical results attained early in the course of the undertaking, despite the handicap of the inefficient physical modalities then available, we decided that future researches should be directed along two separate but related routes, namely, toward the development of simpler, safer, and more easily controllable apparatus for the production of fever, and toward an exploration of the possible fields of usefulness for this mode of therapy.

After some years of experimentation with such modalities as hot baths, hot-air cabinets, electric blankets, diathermy electrical currents, and ultra high-frequency electrical currents (radiotherm) we, with the indispensable collaboration of Dr. Charles F. Kettering and Mr. Edwin C. Sittler, ultimately devised an air-conditioned apparatus which fulfilled the require-

ments at which we had aimed.[5] Eighty of these units were lent to 26 research centers for the purpose of widening the scope of the investigation. The physicians and nurses charged with the responsibility of properly administering the treatments in the various collaborating institutions received special training from us before the apparatus was released for their use.

Coincident with the early engineering developments related to the apparatus, it was natural that the first clinical applications should be directed towards a determination of the possible usefulness of artificial-fever therapy in the management of dementia paralytica. Wagner-Jauregg's successes with the treatment of this disease with malarial therapy had been widely confirmed. Comparable clinical results had also been obtained in those cases of dementia paralytica in which sustained high fever occurred following inoculations with the organisms of rat-bite fever and of relapsing fever, or following injections of vaccines prepared from typhoid and paratyphoid organisms or from Haemophilus ducreyi, or of heteroproteins such as milk or peptone, or of chemical substances such as sulfur. The early claims for specific, intrinsic merit in malaria inoculata appeared to be no longer tenable. Since the common denominator of this wide variety of agencies was the production of fever, many investigators (Neymann, Osborne, Bierman, Schamberg, Bessemans, Whitney, Carpenter, Warren, Kettering, the authors, and others) were stimulated to search for safer and more easily controlled physical methods for accomplishing the same purpose.

Hence, the first patients treated by us with artificial fever, produced by means of various physical modalities, were those who were suffering from dementia paralytica. Despite the difficulties and discouragements encountered in the quest for suitable physical methods, it was observed from the start that the clinical results were at least comparable to those previously obtained by us and by others with malarial therapy.

Since the experiences of many workers with malarial therapy provided unmistakable evidence of the advantages of combining chemotherapy with malarial therapy, and since our results in a small group of patients treated with fever therapy alone were distinctly inferior, we have utilized the combined fever-chemotherapy method practically from the outset.

One advantage of the artificial-fever method in contrast to malarial therapy is that arsenic and bismuth compounds may be administered with each fever treatment. Our observation (*11*) that fever appeared to exert

[5] Because the demands from other institutions exceeded our ability to supply them with this apparatus, an agreement for its manufacture was made with a reliable manufacturer of physical therapy apparatus. This apparatus is sold at a reasonable cost to qualified institutions only (not to private practitioners) with the stated provision that the physicians and nurses who are to engage in the work must receive adequate preliminary training at an approved institution. During the past 2½ years one or more hyperthems have been installed in qualified hospitals in the United States at the rate of one installation per week. Scores of other hospitals in this country and abroad have installed other types of equipment for artificial-fever therapy.

a protective function against anaphylactic phenomena produced in sensitized individuals by arsenic, led us to change from the practice of injecting the arsenical compound half an hour before each fever treatment was begun to that of making the injection when the rectal temperature first reached the level of 105° F. (40.6° C.); this was ordinarily about 75 to 90 minutes after the fever session was started. By this procedure it was possible to abolish, or to minimize greatly, arsenical reactions in patients known to be highly sensitized to this substance.

For purposes of comparison, a variety of arsenical compounds has been employed—bismuth arsphenamine sulfonate [bismarsen], tryparsamide, neoarsphenamine, and meta-amino-parahydroxy-phenylarsine oxide [mapharsen]. One significant observation has accrued from this comparative study, namely, that regardless of the type of arsenical compound used and despite the great variation in arsenic content, the time required for clinical remission and for serologic reversal did not vary appreciably. Factors other than quantitative arsenic-content appear to operate in producing a favorable outcome. During the past 4 years (since February 1937), we have used mapharsen (usually in individual doses of 0.06 gram) to the exclusion of other arsenical compounds. Our experiences confirm those of the many investigators who have found mapharsen to be less toxic than most other available compounds and to produce at least equal clinical and serologic responses.

Just before each fever treatment was commenced the patient received an intramuscular injection of 4 grains of bismuth salicylate.

During the first 6 years of this investigation, the usual course of treatment for neurosyphilitic patients consisted of 10 5-hour sessions of artificial-fever therapy at 105° to 106° F. (40.6°–41.1° C.), with an optimum level of 105.8° F. (41° C.), usually at weekly intervals, for a total of 50 hours. This more or less arbitrary selection of height and duration of fever was based upon an analysis of the results that had been obtained with malarial therapy, which revealed that the proportion of remissions was greatest in those paretic patients who experienced approximately this amount of fever following malaria inoculation.

After the course of combined bismuth-arsenic-fever therapy was completed, the patients received an additional course of bismuth and arsenic injections, given concurrently, at weekly intervals for a period of 20 weeks.

The observation that most paretic patients appeared to experience maximum improvement after the first five or six 5-hour fever sessions led us, in 1937, to experiment with a reduction in the total number of hours of fever together with a decrease in the number of hours per treatment. A comparison of clinical and serologic responses by both procedures revealed no essential differences. Consequently, the usual course of fever therapy during the past 4 years has consisted of 12 3-hour sessions at an average temperature level of 105.8° F. (41° C.), or a total of 36 hours of fever

therapy at this level. Furthermore, it has been found advantageous and equally efficacious to administer fever therapy at more frequent intervals, Thus, patients from distant cities who cannot commute at weekly intervals. were usually hospitalized and received three fever treatments during each week for 4 weeks. No difficulties have arisen from this program, either as a result of shortening the interval between treatments or from the more frequent administration of chemotherapy. Most of the patients were from Dayton or the immediate vicinity. Practically all of the local patients were treated on an ambulatory basis at semiweekly or weekly intervals. The only exceptions were those who required continuous hospitalization during the course of treatment because of physical or mental complications. The advantages of this latter program of shorter sessions at more frequent intervals are that it is possible for one nurse-technician to treat two patients each day, it reduces the cost of the treatments, and it furthers the program of ambulatory care.

Individualization of the therapeutic program according to the status of the patient under treatment is of paramount importance. Most patients being treated for neurosyphilis can tolerate 3 hours of fever at 105°-106° F. (40.6°–41.1° C.) with no difficulty. Markedly debilitated patients, those in the upper age-brackets and those with manifestations of mental deterioration constitute a group which ordinarily would be considered poor risks for either malarial or artificial-fever therapy. It has been our practice to administer artificial fever to such patients in shorter sessions at a lower temperature level in the beginning, increasing the height and length of fever as the course of treatment progresses. In this manner we have been able with minimal risk to afford a large group of patients the benefits of a course of artificial-fever therapy combined with chemotherapy. By such individualization it has been possible to extend treatment to advanced tabetic patients and to deteriorated paretic patients in whom ordinarily little is to be expected in the way of clinical improvement. The results have fully justified the additional effort. For the first treatment they are subjected to one hour of fever at 102°–103° F. (38.8°–39.4° C.). If this is well tolerated, the next treatment whether weekly or semiweekly, is given for one hour at 103°–104° F. (39.4°–40.0° C.). The fever is increased during the next treatment to 104°–105° F. (40.0°–40.6° C.) and finally to 105°–106° F. (40.6°–41.1° C.). When the desired height is reached, the length of the fever session is gradually increased until we are able to give 3 hours of fever at 105°–106° F. (40.6°–41.1° C.). If at any time the patient should display evidence of intolerance to the treatment, either the same length and height of fever or a shorter session at a lower temperature level is given at the next treatment. The average patient is usually able to tolerate the full 3-hour session at 105°–106° F. (40.6°–41.1° C.) after three or four of the short sessions at lower levels. This individualization has been rendered more feasible by the improvements in apparatus and in technic.

Since 1931, we have subjected 1,139 patients to artificial-fever therapy. Of this number, 376 patients have been treated for various manifestations of syphilis. [6] With one possible exception, no patient was harmed by the treatments save for the occasional occurrence of mild skin burns during the early phase of the work. With the improvements in the apparatus this hazard has been entirely eliminated. We have not observed a single instance of skin burn during the course of artificial fever treatments for over 4 years. Even erythema of the skin no longer occurs.

The single exceptional case in which death occurred was that of a 37-year-old man, who was suffering from fulminating meningovascular syphilis and rapidly progressing blindness due to optic atrophy. He had had hypertension for an undetermined period and the history suggested well advanced cerebral vascular sclerosis. At the insistence of the patient and his physicians and with full recognition on the part of all concerned as to the unusual gravity of the situation, the patient was given cautiously a single fever treatment of 4 hours' duration. At the conclusion of the treatment his general condition was good. Seven hours later it was noted that he was somewhat confused and that there was beginning paralysis of the right extremities. By the next morning the hemiparesis was complete, and the patient lapsed into unconsciousness. He died the second day after the fever treatment, probably as the result of cerebral hemorrhage. Permission for post mortem examination was denied.

Only those patients who have been under observation for periods of from 18 months to 9 years and 4 months are considered in this report. Furthermore, the results of therapy as stated in this report refer only to the response attained after a single course of combined artificial fever and chemotherapy. Those patients who did not improve following the usual course, but who attained varying degrees of improvement following a second course, will be considered separately.

The records of 75 syphilitic patients, or 20 percent of the total number of those treated for this disease, are incomplete as a result of the failure of these patients to return at regular intervals for clinical and serologic reexaminations for at least 2 years following the course of therapy. It is known that many of these persons were benefited, at least for periods of several months, by the course of treatment. Many of those who obtained improvement failed to return, despite the urgent pleas of physicians and social workers, because they could not be convinced that it was necessary. A majority of the patients have been observed at regular intervals for over 4 years.

Of 208 patients treated by us for neurosyphilis, the records of 43 (20.6 percent) were excluded from consideration because of incomplete post-

[6] Most of the remaining patients were treated for gonococcic infection, certain forms of infectious arthritis, Sydenham's chorea, rheumatic fever, nonspecific ocular infections, or undulant fever.

therapy observation. Thus, the records of 165 neurosyphilitic patients fulfill the necessarily rigid criteria for critical analysis. These include 65 patients with dementia paralytica, 27 with the tabetic form of dementia paralytica (taboparesis), 29 with tabes dorsalis, 6 with meningeal neurosyphilis, 11 with vascular neurosyphilis, 9 with meningovascular neurosyphilis, and 18 with asymptomatic neurosyphilis (table 4).

TABLE 4.—*Neurosyphilis. Response to combined artificial fever-chemotherapy*

Type of neurosyphilis	Number treated	Incomplete follow-up data	Included for analysis	Remission	Improved	Not improved	Progressed	Blood			Spinal fluid		
								Became negative	Less +	Unchanged	Became negative	Less+	Unchanged
Dementia paralytica (mild)	27	5	22	21	-----	1	-----	13	8	1	13	7	2
Dementia paralytica (intermediate)	37	8	29	21	2	3	3	5	23	1	5	21	3
Dementia paralytica (severe)	17	3	14	2	6	3	3	3	6	5	2	7	5
Tabetic form of dementia paralytica	32	5	27	17	3	5	2	10	11	6	10	10	7
Tabes dorsalis (mild)	6	2	4	4	-----	-----	-----	3	1	-----	2	1	1
Tabes dorsalis (intermediate)	26	10	16	9	4	3	-----	8	4	4	8	2	6
Tabes dorsalis (severe)	15	6	9	2	4	1	2	4	3	2	5	2	2
Meningeal neurosyphilis	6	0	6	5	1	-----	-----	4	1	1	5	1	----
Vascular neurosyphilis	12	1	11	4	1	4	2	3	7	1	3	6	2
Meningovascular neurosyphilis	10	1	9	8	-----	1	-----	4	4	1	5	4	----
Asymptomatic neurosyphilis	20	2	18	11	5	2	-----	11	6	1	11	5	2
Total	208	43	165	104	26	23	12	68	74	23	69	66	30
Percent	-----	20.6	-----	63	16	14	7	41	45	14	42	40	18

Dementia paralytica.—The 65 patients treated for dementia paralytica were grouped according to the classification (described previously) adopted by the Committee on Nonspecific Therapy of Syphilis of the United States Public Health Service, as "mild," "intermediate," or "severe." Similarly, in the appraisal of the results of therapy, the criteria adopted by this committee were employed. The median age of patients treated for dementia paralytica was 37.8 years. All but 15 of the 65 paretic patients had received presumably adequate chemotherapy prior to the institution of artificial-fever therapy; the others had received insignificant amounts of chemotherapy or none.

Included for analysis were the clinical and serologic data on 22 patients with "mild" dementia paralytica. Further proof of the necessity for treating paretic patients during this early stage of the disease is found in the fact that 21 of the 22 patients (95 percent) achieved remission; one patient was not improved. In those treated for "mild" paresis the blood serologic reactions were reversed to negative in 13 patients (59 percent), became less

positive in 8 additional patients (36 percent), and were not influenced in 1 patient (5 percent). The spinal fluid serologic reactions became negative in 13 patients (59 percent), were less positive at the time of last observation in 7 patients (32 percent), and remained positive in 2 patients (9 percent).

Of the 29 patients with "intermediate" dementia paralytica, 21 (72 percent) obtained remission; 2 patients (6 percent) were improved. Thus 78 percent of those with "intermediate" paresis were benefited. Three patients in this group were not improved, and the disease progressed following treatment in 3 additional patients. The blood serologic reactions were reversed to negative in 5 patients (17 percent) of those with "intermediate" paresis, became less positive in 23 patients (79 percent), and remained positive in 1 patient (4 percent). The spinal fluid serologic reactions were changed to negative in 5 patients (17 percent), were less positive at the time of the last reexamination in 21 patients (73 percent), and remained positive in 3 patients (10 percent).

As would be anticipated, the proportion of favorable clinical responses to the combined method of fever-chemotherapy was distinctly less in the patients with "severe" paresis. Thus, of 14 patients in this advanced stage of the disease, only 2 (14 percent) achieved clinical remission. Six additional patients (43 percent) were improved. In 3 patients there was no improvement, while in 3 others the disease progressed despite treatment. It is perhaps of importance to indicate, however, that even in patients with manifestations of advanced paresis considerable salvage was effected. Over one-half of the patients in this category were benefited. The responses of the blood and spinal fluid reactions exhibited no constant relationship to the clinical outcome. The reactions remained strongly positive in some who achieved clinical remission, and were reversed to negative in some in whom the disease process either was uninfluenced or progressed. The serologic reactions of the blood became negative in 3 patients (21 percent), became less positive in 6 patients (43 percent), and remained positive in 5 (36 percent). The spinal fluid serologic reactions were reversed to negative in 2 patients (14 percent), became less positive in 7 patients (50 percent), and were still positive at the time of the last observation in 5 patients (36 percent).

Tabetic form of dementia paralytica (taboparesis).—In the group of 27 patients with the tabetic form of dementia paralytica (taboparesis) the symptoms and signs of paresis usually dominated the clinical picture. All but one had received varying amounts of chemotherapy prior to artificial-fever therapy. While many of these patients achieved coincidental improvement in both tabetic and paretic manifestations, the clinical outcome of therapy was largely dependent upon the relative mildness or severity of the paretic symptoms. Since it was not considered feasible to classify such patients in "mild," "intermediate" or "severe" categories because of the great variation in the relative degrees of paretic and tabetic symptoms,

they are considered as one group. The prompt relief of lightning pains and gastric crises was the outstanding feature of the response to treatment; 3 patients experienced recurrence of root pains which yielded to additional fever-chemotherapy. Those with ataxia of short duration usually experienced some improvement in gait. Three patients with cord bladder regained control of bladder function; one advanced taboparetic with cord bladder was not benefited.

Seventeen of the twenty-seven taboparetic patients (63 percent) achieved clinical remission of both tabetic and paretic symptoms. Three additional patients (11 percent) were improved. Thus, 20 of the 27 patients (74 percent) in this group responded favorably. Five patients with severe paretic symptoms were not improved, and the disease progressed during and after treatment in two demented patients, who died 6 months and 1 year, respectively, after the course of treatment was completed.

The blood serologic reactions were reversed to negative in 10 patients (37 percent), became less positive in 11 patients (41 percent), and were not influenced in 6 patients (22 percent). The spinal fluid serologic reactions were reversed to negative in 10 patients (37 percent), became less positive in 10 patients (37 percent), and remained unchanged in 7 patients (26 percent).

Tabes dorsalis.—All of the 29 patients with tabes dorsalis had received varying amounts of chemotherapy before artificial-fever therapy was begun. Included in this group of patients were 4 with "mild" tabetic manifestations,[7] such as lightning pains of recent origin, paresthesias, pupillary disturbances, reduced or exaggerated reflexes, or diplopia. There were 16 patients with "intermediate" tabes dorsalis, in which group were included those manifesting the signs and symptoms mentioned above, together with such additional evidence as cord bladder, early and mild ataxia, gastric crises, or early optic atrophy. The 9 patients with "severe" tabes dorsalis exhibited such manifestations as marked ataxia, severe lightning pains or gastro-intestinal crises or both, incoordination, cord bladder, marked hyperesthesias or paresthesias, optic atrophy, or Charcot's joints. Most of the patients with "severe" tabes dorsalis presented themselves with evidences of advanced malnutrition and avitaminosis; many verged on starvation because of almost uninterrupted gastro-intestinal crises. These patients presented the most trying treatment problems. Most would not have been considered as candidates for either malarial therapy or artificial-fever therapy a few years ago. With the improvements in the apparatus for the production of fever and in the technic of administering the treatments, a significant proportion of these patients may be helped, particularly in relief from the lightning pains or from the gastro-intestinal crises. Such patients are first given short, trial fever treatments, at a low fever level, following three or four of which it is usually possible to give the usual 3-hour sessions

[7] Classification of Committee on Nonspecific Therapy of U. S. Public Health Service.

at 105.8° F. (41° C.). Correction of dietary deficiencies, of anemia, and often of narcotic addiction are essential requirements in the therapeutic program.

It is unfortunate that the use of fever therapy is still too often regarded as a final, resortive method of treatment. Much better results will be achieved when it is more generally recognized that fever therapy combined with chemotherapy is the primary treatment of choice in all types of symptomatic and asymptomatic neurosyphilis. This fact is particularly apparent in the management of patients with tabes dorsalis.

Of the 4 patients with "mild" tabes dorsalis, all obtained prompt and lasting remission. The lightning pains or gastro-intestinal crises, or both, often responded after the first two or three treatments. There has been no recurrence of such pains in the patients with "mild" tabetic symptoms; additional treatments were not required in this group of patients. The blood serologic reactions of the "mild" tabetic patients were reversed to negative in 3 patients (75 percent) and in the fourth patient (25 percent) became less positive. The spinal fluid serologic reactions became negative in two patients (50 percent), were less positive at the time of the last reexamination in 1 patient (25 percent), and remained unchanged in 1 patient (25 percent).

Nine (56 percent) of the sixteen patients with "intermediate" tabes dorsalis obtained clinical remission following one course of combined fever-chemotherapy. The most striking result of treatment was the prompt and persistent disappearance of the lancinating pains and gastro-intestinal crises. In 3 patients with mild and early ataxia the gait was restored to normal. Four (25 percent) of the patients with "intermediate" tabes dorsalis obtained improvement. Three of these patients experienced recurrence of root pains, which were controlled with additional fever-chemotherapy. Two patients with cord bladder regained normal control of bladder function. Some improvement in gait disturbance occurred in all of the patients in this group. Three patients (19 percent) with "intermediate" tabes dorsalis were not benefited by the course of treatment. The blood serologic reactions were reversed to negative in 8 (50 percent) of the patients with "intermediate" tabes dorsalis, became less positive in 4 patients (25 percent) and were uninfluenced in 4 patients (25 percent). The spinal fluid serologic reactions were reversed to negative in 8 patients (50 percent), became less positive in 2 patients (12.5 percent), and were unchanged in 6 patients (37.5 percent).

The results of treatment were decidedly inferior in the group of 9 patients with "severe" tabes dorsalis. Remission occurred in only 2 patients (22 percent). Some measure of improvement, including relief of pains or improvement in bladder function, occurred in 4 patients (22 percent). In one patient there was no improvement. In 2 advanced tabetic patients the disease progressed despite treatment, and these patients died of the

disease several months after the completion of the course of treatment. The blood serologic reactions became negative in 4 patients (45 percent), became less positive in 3 patients (33 percent), and were unchanged in 2 patients (22 percent). The spinal fluid serologic reactions were reversed to negative in 5 patients (56 percent), were less positive at the time of the last reexamination in 2 patients (22 percent), and remained unchanged in 2 patients (22 percent).

Meningeal neurosyphilis.—Six patients with meningeal neurosyphilis were treated with combined artificial-fever therapy and chemotherapy. All but one had had presumably adequate chemotherapy. The characteristic manifestations of syphilitic meningitis were present, such as headache, dizziness, diplopia, nausea, vomiting, nuchal rigidity, aphasia, or convulsions, associated with the typical spinal fluid changes (pleocytosis, increased protein content, and strongly positive serologic reactions). Five of the six patients (83 percent) experienced complete clinical recovery; the sixth patient was relieved of all symptoms and signs except residual diplopia. The spinal fluid cell count was promptly reduced to normal levels in all; the protein content of the spinal fluid exhibited a similar but invariably slower reduction to normal levels. The blood serologic reactions were reversed to negative in 4 patients (67 percent), became less positive in one patient, and remained positive in another. The spinal fluid serologic reactions were favorably influenced in all; there was reversal to negative in 5 (83 percent) and reduction in positivity in one (17 percent).

Vascular neurosyphilis.—Twelve patients received combined artificial fever and chemotherapy because of vascular neurosyphilis. The records of 11 patients are complete to date; the twelfth patient disappeared shortly after having attained an apparently favorable response to treatment. Of the 11 patients whose records are included in the analysis, all but one had received presumably adequate, but ineffectual, chemotherapy prior to the institution of artificial-fever therapy.

The patients classified as having vascular neurosyphilis did not present evidence of meningeal involvement, but presented such subjective and objective manifestations of vascular neurosyphilis as headaches, dizziness, monoplegia, hemiplegia, aphasia, recurrent cerebrovascular accidents in the absence of evidence of arteriosclerosis, or convulsions, together with characteristic spinal fluid changes.

Of the 4 patients (36 percent) who achieved complete remission, 2 had experienced cerebrovascular accidents followed by transient hemiplegia; there has been no recurrence in either patient during the 3- and 5-year intervals which have elapsed since fever-chemotherapy was given. One patient was improved, but some residual hemiplegia has persisted. Four patients (36 percent) were not improved, while in 2 other patients (18 percent) the disease progressed. The blood serologic reactions were reversed to negative in 3 patients (27 percent), became less positive in 7

patients (63 percent), and remained positive in 1 patient. The spinal fluid serologic reactions became negative in 3 patients (27 percent), were less positive at the time of the last reexamination in 6 patients (55 percent), and have remained positive in 2 patients (18 percent).

Meningovascular neurosyphilis.—The 9 patients with meningovascular neurosyphilis whose records are complete exhibited various combinations of meningeal and cerebrovascular manifestations. In some, the vascular component was predominant while in others the meningeal involvement was more pronounced. The meningitic phenomena were promptly and favorably influenced in all. Eight of the 9 patients (89 percent) achieved complete clinical remission; the other patient experienced no improvement in the hemiparesis which had developed 3 months before artificial-fever treatment was began. The blood serologic reactions were reversed to negative in 4 patients (44 percent), became less positive in 4 patients (44 percent), and were unchanged at the time of the last reexamination in 1 patient. The spinal fluid serologic reactions became negative in 5 patients (56 percent) and became less positive in 4 patients (44 percent).

Asymptomatic neurosyphilis.—It is now generally recognized that the best time to treat neurosyphilis with fever-chemotherapy is when the disease is first recognized in its asymptomatic phase. The now more common and eminently desirable practice of performing spinal fluid examinations before, during, and after the course of antisyphilitic chemotherapy has provided indisputable evidence of the high incidence of neurosyphilis. The extensive and carefully documented studies of the Cooperative Clinical Group (*12a*, *b*, *c*) revealed that abnormal spinal fluid conditions were present in 33 percent of patients with early syphilis and in 56.1 percent of patients with late secondary syphilis. The same observers have also stated that "even thoroughgoing (chemical) treatment does not necessarily prevent the development of abnormalities of the spinal fluid" (*12b*) and that in latent syphilis "almost all the serologic response to be expected occurs within the first four months of treatment; thereafter, further (chemical) treatment has little effect" (*12c*). In our experience, the favorable response to combined artificial fever-chemotherapy has been most prompt in those patients who were referred to us for such treatment immediately after the diagnosis of asymptomatic neurosyphilis was first established. All but 4 of our patients with asymptomatic neurosyphilis had had presumably adequate chemotherapy. No patients with so-called "group I" spinal fluid changes (slight to moderate pleocytosis and increase of protein, with negative serologic reactions, and negative colloidal gold curves) are included in our series.

In the 18 patients with asymptomatic neurosyphilis treated by us with artificial fever-chemotherapy, who have been observed at intervals for a sufficiently long period, the spinal fluid serologic reactions, cell count, and protein content have been restored to normal in 11 patients (61 percent).

The serologic reactions of the spinal fluid showed a declining trend at the time of the last observation in 5 additional patients (28 percent). Thus, there was improvement in the serologic status of 16 (89 percent) of these patients. In the remaining 2 patients (11 percent), the spinal fluid reactions were still positive at intervals of 20 months and 27 months, respectively, following the termination of the course of treatment. On the basis of prior experience, there is reason to anticipate that those patients who now exhibit a declining trend in serologic positivity and those more recently treated patients whose reactions are still positive will ultimately obtain a successful result. No patient who achieved serologic reversal has experienced either serologic relapse or any evidence of symptomatic neurosyphilis.

The responses in the blood serologic reactions closely paralleled those in the spinal fluid. In 11 patients (61 percent) negativity was achieved. Six additional patients (33 percent) exhibited less positive reactions, while 1 more-recently treated patient had unchanged positive reactions at the time of the last observation.

It seems axiomatic to state, therefore, that the best treatment for neurosyphilis is to detect it in its incipiency and to prevent the later development of its disastrous sequels by the prompt administration of some form of fever therapy combined with chemotherapy.

In sum, it is interesting to note that the remission rate of all of the 165 well-documented cases of various types of neurosyphilis was 63 percent. An additional 16 percent of patients were improved by the treatment. Thus, a total of 79 percent of the patients were benefited.

OCULAR SYPHILIS

ONE OF THE DISASTROUS consequences of syphilis is blindness. This disease has been held responsible for at least 10 percent of blindness occurring throughout the world. In many cases the ocular manifestations of syphilis are but one associated incident in patients with secondary syphilis, neurosyphilis, visceral syphilis, cutaneous syphilis, or osseous syphilis. In the cases studied by us, 63 of the 103 patients (61 percent) with ocular syphilis had associated manifestations of syphilis elsewhere in the body, chiefly in the central nervous system.

The fact that a high proportion of patients with ocular syphilis have failed to respond to vigorous, continuous chemotherapy (arsenical, bismuth, mercurial, and iodide compounds) has engendered an attitude of pessimism in the minds of many ophthalmologists and syphilologists. Such a spirit of hopelessness and indecision is no longer justified. Similarly, procrastination with chemotherapy may often rob the patient with ocular syphilis of his chance for the preservation of useful vision.

Following the advent of malarial therapy it was soon apparent that considerable salvage could be accomplished in cases of refractory ocular syphilis. Typhoid-paratyphoid vaccine and other foreign protein substances have also been used widely; even though favorable clinical responses have often followed the use of these fever-producing agencies, severe reactions have occurred and the febrile response is uncertain and frequently is inadequate. Many of our patients with ocular syphilis who had not been benefited by repeated injections of typhoid or T. A. B. vaccine responded well to subsequent artificial-fever therapy.

Of the 103 patients treated by us for various manifestations of ocular syphilis, 19 failed to return regularly for clinical and serologic reexaminations. The syphilitic ocular diseases of the 84 patients were classified as follows: Exudative uveitis, 10 patients; neuroretinitis and optic neuritis, 13 patients; choroiditis, 10 patients; interstitial keratitis, 21 patients; optic atrophy, 25 patients; and extra-ocular palsy, 5 patients.

EXUDATIVE UVEITIS

All of the 10 patients with exudative uveitis had received chemotherapy previously. In 6 instances the uveitis occurred while the patients were receiving continuous antisyphilitic therapy. Two patients had received intravenous injections of typhoid vaccine without benefit. In 7 of the patients there was so much exudate in the anterior segment that it was impossible

to distinguish details of the fundus. Major impairment of vision seemed inevitable in all. After the first or second fever treatment there was distinct diminution in the degree of ciliary injection and in the amount of exudate, accompanied by improvement in the dilatation of the pupil and in relief of symptoms.

There was marked clinical improvement in 7 (70 percent) of the 10 patients. The response in these patients was rapid, and residual visual defects were either absent or were of minor degree. In the 3 remaining patients (30 percent), the inflammatory manifestations responded promptly, but there remained varying degrees of visual impairment. All, however, retained useful vision. There have been no recurrences.

McGavic (*13*) has reported similarly favorable responses in 11 patients with iridocyclitis treated with artificial-fever therapy (Kettering hypertherm) combined with chemotherapy.

OPTIC NEURITIS AND NEURORETINITIS

In 2 of the 13 patients with optic neuritis and neuroretinitis this ocular complication occurred while they were receiving chemotherapy for secondary syphilis. Eight patients had some form of syphilis of the central nervous system. All but 2 had received varying amounts of chemotherapy. As in the cases of uveitis, there was prompt diminution in the amount of exudate in the fundus. Two patients had associated choroiditis, and one also had exudative uveitis which responded equally well. All of the patients in this group recovered useful vision, although 8 retained some residual pallor of the disk and slight contraction of the visual fields. Active neuritis along the optic tract appears to be arrested by fever therapy.

CHOROIDITIS

The manifestations of choroiditis responded promptly in the 10 patients with this ocular complication of syphilis. All had failed to respond to chemotherapy. The average time for the disappearance of the exudate was 6 weeks, which was somewhat longer than in the cases of uveitis and neuroretinitis. Fortunately, none of the lesions involved the macula; hence, central vision was retained in all. Recurrence of choroiditis has not been observed in these patients following the course of combined fever-chemotherapy.

INTERSTITIAL KERATITIS

The ages of the 21 patients suffering from interstitial keratitis varied from 8 to 38 years. All but 4 had been treated unsuccessfully with chemotherapy before fever therapy was instituted. Nine patients had experienced from 1 to 8 previous attacks. The response to combined fever-chemotherapy was most prompt and favorable in those cases in which an opaque central disk of plastic exudate was present. It is usually this type of the disease which produces the greatest visual damage because it commonly

leaves the center of the cornea permanently and densely opaque. While there was prompt relief of pain, blephorospasm, lacrimation, and photophobia, the clearing of the corneal stroma occurred more slowly. The response was best in the acute stage of the disease and when there was considerable exudation into the corneal stroma. While varying amounts of corneal scarring were present in several patients, depending largely upon the duration of the disease and the number of prior recurrences, there was little doubt that the more prompt resolution of the active inflammatory phase of the disease by fever therapy minimized the extent of the residual scarring. Only 1 patient has experienced a mild recurrence of interstitial keratitis, which responded promptly to additional fever-chemotherapy. Hence, it was concluded that the duration of this disease and the tendency toward recurrence are distinctly lessened following adequate artificial fever-chemotherapy.

OPTIC ATROPHY

Optic atrophy occurred chiefly as an accompaniment of tabes dorsalis, or less often, of dementia paralytica. The visual acuity and the visual fields have remained practically unaltered following fever-chemotherapy in the 25 patients with optic atrophy. Since, without treatment, blindness often results within 2 or 3 years of the onset of primary optic atrophy, it is significant that the progression of the disease was apparently retarded by fever-chemotherapy. There is also some justification for the impression that if optic atrophy is associated with foci of active inflammatory infiltrations along the optic tract, such exudative lesions will respond to fever therapy.

Moore (*14*) expressed the belief that fever therapy is especially of value when the optic atrophy is associated with paresis or taboparesis. In an analysis of the results obtained by 11 different observers, Moore found that of 89 patients treated with fever therapy, the optic atrophy improved or remained stationary in 39 percent and was unimproved or progressed in 61 percent. Mcnagh (*15*) found that 4 of 10 patients with optic atrophy experienced visual improvement following artificial-fever therapy combined with chemotherapy.

EXTRA-OCULAR PALSY

Of the five patients with extra-ocular palsy, only two showed any degree of improvement following fever-chemotherapy; the other three were not benefited. There was no evidence, therefore, that artificial-fever therapy is superior to older methods of treatment in cases of extra-ocular palsy.

From the observations made on patients with ocular syphilis, it seems apparent that those syphilitic lesions which are characterized by exudate respond promptly and well to combined artificial fever-chemotherapy. In the interest of preserving vision, patients presenting such exudative manifestations should receive fever-chemotherapy as soon as possible after the diagnosis is established.

RESISTANT SEROPOSITIVE LATENT SYPHILIS

IN AN EFFORT to determine the effect of artificial fever combined with chemotherapy on persistently positive blood serologic reactions, 51 patients with so-called "Wassermann-fast" latent syphilis have received the same course of combined therapy as that used for neurosyphilis (table 6). All had had presumably adequate chemotherapy for at least 2 years. The records of 7 patients are incomplete; only those patients who were observed for at least 2 years following the completion of the combined course of fever-chemotherapy are considered in this analysis. Of the 44 patients whose records are satisfactory for analysis, 17 had had syphilis for from 2 to 4 years, while the remaining 27 patients had had the disease more than 4 years. The spinal fluid serologic reactions in all were negative. Of the 17 patients with early latent syphilis with resistant seropositive reactions, the blood serologic reactions were reversed to negative in 12 patients (70 percent) and became less positive in 5 patients (30 percent). Of the 27 patients with seropositive late latent syphilis, the blood serologic reactions were reversed to negative in 13 patients (50 percent), became less positive in 10 patients (38 percent), and remained positive in 4 patients (12 percent). No patient who achieved serologic reversal has exhibited either serologic or clinical relapse.

EXPERIMENTAL TREATMENT WITH COMBINED FEVER-CHEMOTHERAPY

BEFORE ENTERING upon any discussion of the possible application of artificial-fever therapy combined with chemotherapy to primary and secondary syphilis it would be pertinent to emphasize the purely experimental character of the undertaking. While the results attained by other workers and by us are sufficiently encouraging to justify, or even to demand, continued and vigorous inquiry over a period of several years, it should not be inferred that this mode of therapy is recommended at this time as a substitute for the tried-and-proved schema of continuous chemical treatment in the mass-management of early syphilis.

Candor requires, however, that recognition be given to the fact that even the generally approved methods of continuous chemical therapy possess serious, and often insuperable, handicaps. Not the least of these are the strong social and economic forces which operate to keep large numbers of persons with early syphilis from receiving adequate therapy. The sound and vigorous educational campaign launched by Surgeon General Thomas Parran and his associates of the United States Public Health Service has done much to overcome these deterrents. A wholesome dissatisfaction exists even among syphilologists with the present orthodox methods of treatment. Because of the long period required for efficient treatment, the high cost, and the not insignificant number of instances of chemical intoxication, the great majority of syphilitic persons do not receive even sufficient treatment to render them noninfectious to others (*16*). There is convincing evidence that insufficient chemical treatment early in the course of syphilis prevents the development of the natural specific resistance to the disease. To quote Chesney (*17*): "A small amount of treatment in early syphilis is worse than none, precisely because it interferes with the body's own defensive mechanism while at the same time it often fails to eliminate the infection." Padget's (*18*) long-term evaluation of the results of treatment of early syphilis at the Johns Hopkins Hospital led him to state that "the palpable inferiority of irregular and intermittent treatment strongly suggests that, if continuous treatment cannot be given, no treatment is the desideratum."

The deficiencies in the present-day management of syphilis have been stated succinctly and with admirable frankness by Moore (*19*): "It must be recognized that even given more clinics, better clinics, and free clinics,

the control of syphilis by present-day treatment methods is still far from satisfactory. Treatment is too prolonged, too painful, too dangerous, too expensive. Efforts of investigators to develop better and especially shorter methods of treatment should be encouraged."

A rich background of experimental studies of animals and of human subjects, notably those made by Weichbrodt and Jahnel (*20*), Bessemans (*21*), Schamberg and Rule (*22*), Carpenter, Boak and Warren (*23*), Levaditi and de Rothschild (*24*), Kolmer (*25*), and Simpson (*10l*), provides convincing evidence of the unfavorable influence of high body temperature on Spirochaeta pallida. Bessemans and his associates found that the application of heat to the testicular syphilomata of rabbits, whether by means of hot water baths, hot air blowers, hot paraffin baths or packs, luminous or infrared radiations, electromagnetic induction or air-conditioned chambers, destroyed the spirochete when the temperature in the syphilitic lesion (as measured by small thermocouples) was maintained at 1 hour at 107.6° F. (42° C.), or for 2 hours at 104° F. (40° C.)

Both Schamberg and Bessemans have commented upon the implications of such observations as regards the probable prophylactic value of a prolonged hot bath shortly after exposure to venereal infection. (The gonococcus is even more susceptible to heat.)

Bessemans also found, however, that Spirochaetae pallidae in the popliteal lymph nodes of a syphilitic rabbit rarely lose their virulence if the rabbit is subjected to a sufficiently high body temperature only to destroy the spirochetes in the external lesions. It sometimes required a temperature of 114.8° F. (46° C.) *for 1 hour* to achieve the same result.

On the other hand, Carpenter and his coworkers found that body temperature of 106.7°–107.6° F. (41.5°–42° C.), *maintained for 6 hours*, was uniformly sufficient to destroy Spirochaeta pallida both in the testicles and in the popliteal lymph nodes of syphilitic rabbits. Our animal experiments confirm these findings (*10h*). It is well to point out that the in vivo thermal death time of Spirochaeta pallida will vary with both the height and the duration of temperature. Thus, since the effect is one of thermal gradient, it is erroneous to state that any given temperature level is the thermal death time without adding a qualification as to the length of time the tissue containing the organism was exposed to that temperature. Hence, the in vivo thermal death time of Spirochaeta pallida in the popliteal lymph nodes of syphilitic rabbits is either 114.8° F. (46° C.) when the temperature is applied for 1 hour (Bessemans), or 106.7°–107.6° F. (41.5°–42° C.) when this range of temperature is maintained for 6 hours (Carpenter, Boak, and Warren; Simpson and Kendell). Carpenter and coworkers have also demonstrated that the same spirochetecidal effect is produced at lower temperature levels when applied for longer intervals.

More recently, both the Ghent investigators (Bessemans and coworkers) and those at Rochester (Boak, Carpenter, and Warren) have performed

independently a series of crucial experiments on the concurrent treatment of experimental syphilis in rabbits with artificial fever combined with chemotherapy. When his important work was interrupted by the invasion of Belgium, Professor Bessemans was in the midst of determining whether or not a judicious combination of chemotherapy and artificial-fever therapy might be more effective than either form of therapy used alone in curing syphilis in rabbits. The preliminary experiments revealed that while some lymph-node transfers made from rabbits which had received either chemotherapy alone or artificial-fever therapy alone caused the production of syphilis in normal rabbits, all of the lymph-node transfers from rabbits treated with combined fever-chemotherapy yielded entirely negative results.

The carefully conceived and admirably controlled recent experiments of Boak, Carpenter, and Warren (*26*) were designed to determine the effects produced by combining subcurative chemotherapy with subcurative artificial-fever therapy in experimental syphilis of rabbits. Notwithstanding the fact that many investigators [Kyrle (*27*), Richet and Dublineau (*28*), Simpson and Kendell (*10h, o*), Neymann, Lawless, and Osborne (*29*)] have found convincing clinical and immunologic evidence that fever therapy combined with chemotherapy is more effective than either agent employed singly in the treatment of early syphilis in human beings, the Rochester investigators felt that additional experimental data were needed to establish the combined method as an accepted therapeutic procedure for early syphilis in human subjects. Two strains of Spirochaeta pallida, the Nichols and the Zinsser-Hopkins strains, were employed. Syphilis was produced in chinchilla rabbits by intratesticular injections of a suspension of spirochetes (confirmed by dark-field examination) derived by trituration in a mortar of tissue from the testes and from the popliteal lymph nodes of animals presenting prominent syphilitic lesions.

As soon as unequivocal syphilitic lesions developed (1 to 3 months), 127 rabbits were treated in one of six ways (table 5). Twenty-three of the rabbits received a single subcurative injection of neoarsphenamine (10 milligrams per kilogram of body weight), followed by a single 3-hour fever session at a rectal temperature of 106.7° F. (41.5° C.); all were cured. The criteria of cure were clinical examination for from 1 to 3 months, after which the animals were sacrificed and suspensions of testicular and popliteal lymph-node tissues were injected into normal rabbits; no clinical or serologic evidence of syphilis appeared in these rabbits during a minimum period of 6 months. Further verification of cure was established by the successful transfer of the infection to the normal control rabbits at a later date.

Twenty-one syphilitic rabbits were given the same amount of neoarsphenamine, followed by a 4-hour session of fever, for the purpose of determining the possible advantage of an additional hour of fever; all but one (95 percent) were cured. Thus, of 44 syphilitic rabbits treated with a

single subcurative quantity of neoarsphenamine followed immediately by a subcurative session of fever therapy for 3 or 4 hours, 43 (98 percent) were cured.

For the purpose of comparing the efficacy of the combined treatment when the drug was administered immediately after the fever session rather than before, 20 syphilitic rabbits were given a 3-hour session of fever at the same level, followed by an injection of the same quantity of neoarsphenamine; the results were distinctly inferior—only 15 (75 percent) were cured.

TABLE 5.—*Effects on experimental syphilis in rabbits of concurrent treatment with neoarsphenamine and artificially induced fever at 106.7° F. (41.5° C.)*

[Boak, Carpenter, and Warren, University of Rochester, Rochester, N. Y.]

Treatment	Number of animals	Number cured	Percent cured
TESTS			
Experiment 1: 10 milligrams of neoarsphenamine per kilogram of body weight, followed immediately by a 3-hour fever at 106.7° F. (41.5° C.)	23	23	100
Experiment 2: 10 milligrams of neoarsphenamine per kilogram of body weight, followed immediately by a 4-hour fever at 106.7° F. (41.5° C.)	21	20	95
Experiment 3: 3-hour fever at 106.7° F. (41.5° C.), followed by the intravenous injection of 10 milligrams of neoarsphenamine per kilogram of body weight	20	15	75
CONTROLS			
Untreated (to test for spontaneous cure)	14	0	0
10 to 20 milligrams of neoarsphenamine per kilogram of body weight (no fever)	10	3	33
5-, 6-, or 7-hour fever at 106.7° F. (41.5° C.); no neoarsphenanime	39	4	10

Fourteen syphilitic rabbits received no treatment as a control test for spontaneous cure; all remained infected. Tissue transfers made from these animals invariably resulted in the infection of normal rabbits. Ten control rabbits received only a single injection of neoarsphenamine, ranging in dosage from 10 to 20 milligrams per kilogram of body weight; only 3 (33 percent) were cured. As a control on the subcurative effect of either a 3-hour or 4-hour session of fever alone, 39 rabbits received 5-, 6-, or 7-hour sessions of fever (without neoarsphenamine); only 4 (10 percent) were cured.

It is, then, quite apparent that a mode of therapy which combines a subcurative dose of neoarsphenamine with a subcurative session of artificia fever gives superior results in the treatment of experimental syphilis in

rabbits when compared with the administration of greater amounts of the drug, or of fever alone. The time of administration of the antisyphilitic drug in relation to the fever is particularly significant. The results were distinctly better when the drug was administered immediately prior to, rather than immediately after, the fever session. It is probable that one of two factors, or both, operate in producing this favorable effect, namely, the more widespread distribution of the drug as the result of increased blood velocity and capillary dilatation, and the increase in the spirocheticidal effect of the chemical substance as a result of the elevation in body temperature. Eagle (*30*) has demonstrated that the antispirochetal action (in vitro) of both arsenic and bismuth compounds is increased approximately twofold with a 10° C. rise in temperature. Thus, it is probable that the minimal effective concentration of these chemical compounds is less when the body temperature is elevated to an effective level.

In collaboration with Dr. Robert A. Kehoe and his associates at the Kettering Laboratory of Applied Physiology, University of Cincinnati, we are engaged in an investigation of the in vivo minimum effective concentration of antisyphilitic chemical compounds in the blood, spinal fluid, and tissues of animals and of human beings, with and without fever therapy.

PERSONAL EXPERIENCES WITH COMBINED FEVER-CHEMOTHERAPY IN EARLY SYPHILIS

Our interest in the possibilities of utilizing artificial-fever therapy as an adjunct to chemotherapy in the management of early syphilis was first aroused by the observations that (a) the best results of combined fever-chemotherapy occurred in patients with the earliest manifestations of neurosyphilis, (b) that the most prompt and satisfactory results occurred in such patients when even small doses of chemotherapeutic compounds were administered simultaneously with fever therapy, (c) that mucocutaneous or osseous lesions which had previously resisted chemotherapy usually responded promptly when fever therapy was added to the usual therapeutic program, (d) that chemoresistant seropositive latent syphilis often yielded to the combined therapy, and (e) that fever apparently exerted a protective function against sensitization reactions when arsenical compounds were injected at the height of fever. Thus it appeared that artificial-fever therapy fortified and intensified the action of antisyphilitic chemical agents. The accumulated evidence of the thermolability of Spirochaeta pallida in experimental syphilis in animals provided further encouragement to launch such studies in human beings, with full recognition of the fact that syphilis in rabbits and syphilis in human beings behave quite differently.

Consequently, since 1932, we have subjected 77 patients with primary or secondary syphilis to the same course of combined artificial fever and chemotherapy as that employed in cases of neurosyphilis. During the first 6

years the usual course of fever therapy consisted of approximately 50 hours of fever at an average temperature of 105.8° F. (41° C.), usually given in 10 weekly sessions of 5 hours each. Since 1937 such patients have received an average of 12 shorter sessions (3 hours) of fever usually at more frequent intervals (twice or thrice each week), for an average total of 36 hours of sustained fever at the same average temperature level of 105.8° F. (41° C.). No essential differences in either clinical or serologic responses were observed in the two groups.

At the outset of the experiment, it was decided to institute control studies to determine the efficacy of fever therapy alone and of chemotherapy alone of the same amount and kind as that used in patients treated by the combination of the two methods. After 6 patients with primary or secondary syphilis had been treated solely with a total of 50 hours of fever therapy, it was deemed unwise to continue with this part of the experiment since in 2 of the patients clinical relapse developed; all were then given continuous chemotherapy. In the second control group of 15 patients with primary or secondary syphilis in which 30 concurrent injections of the arsenic and bismuth compounds were given, 4 exhibited clinical relapse. It was quite apparent, therefore, that fever therapy alone or chemotherapy alone, as applied to these control groups, was inadequate.

Of the 77 patients treated for early syphilis with combined fever-chemotherapy, the records of 17 patients are incomplete for lack of adequate posttherapy observation. The 60 patients who have been reexamined clinically and serologically at frequent intervals were classified as follows: Seronegative and dark-field positive primary syphilis, 8 patients; seropositive primary syphilis, 24 patients; early secondary syphilis, 20 patients; late secondary syphilis, 8 patients (table 6). The period of observation following the combined course of treatment has varied from 2 years to 9 years.

TABLE 6.—*Primary, secondary and latent syphilis response to combined fever-chemotherapy*

Type of syphilis	Number treated	Incomplete follow-up data	Included for analysis	"Cured"	Improved	Not improved	Blood		
							Became negative	Less positive	Unchanged
Seronegative primary	9	1	8	8					
Seropositive primary	31	7	24	22	[1] 2		24		
Early secondary	27	7	20	18	[2] 2		20		
Late secondary	10	2	8	4	[3] 3	1	5	3	
Early latent	19	2	17				12	5	
Late latent	32	5	27				13	10	4

[1] 2 patients required additional fever-chemotherapy.
[2] 2 patients required additional fever-chemotherapy.
[3] 3 patients required additional fever-chemotherapy.

Seronegative, dark-field positive primary syphilis.—Positive serologic reactions did not develop either during or following the course of combined therapy in any of the eight patients with seronegative, dark-field positive primary syphilis. None of the patients had received any previous chemotherapy. No living spirochetes could be demonstrated in the chancres after the first treatment. The average healing time of the chancres was 2 weeks.

Seropositive primary syphilis.—With two exceptions, the 24 patients with seropositive primary syphilis exhibited a rapid and progressive decline of the serologic reactions to negativity. The Kahn quantitative procedure was found to be of indispensable value in measuring the degree of serologic response and in determining the need for additional therapy in these patients. In the two exceptional cases additional fever-chemotherapy was given because complete serologic negativity was not attaincd after the single course. The Kahn quantitative units remained stationary at 40 units in one case and exhibited an increase from 40 to 360 units during the 10 months following therapy in the other case. Both patients achieved serologic negativity following a second course of fever-chemotherapy.

Secondary manifestations during first year of disease.—Of the 20 patients with early secondary manifestations of syphilis (occurring during the first year of the disease), 14 had received no previous chemotherapy, while 6 had had varying amounts before combined fever-chemotherapy was instituted. It was soon apparent that both the clinical and serologic responses were much more prompt and complete in those who had not received prior chemotherapy. It is also true that those who had had previous chemotherapy were referred to us for fever therapy because of their failure to respond to chemotherapy in thc usual manner; hence these patients probably represented an unusually resistant type.

All but 2 of thc 20 patients achieved serologic negativity during or soon after the completion of the combined course. The two refractory patients required additional fever-chemotherapy before the serologic reactions were reversed to negative. In one patient in this group exfoliative dermatitis had developed following injections of neoarsphenamine. Full adult doses of bismarsen were tolcrated by this patient without incident when the injections were given in conjunction with the fever sessions. During the follow-up course of bismarsen injections exfoliative dermatitis again developed. Thc Kahn quantitative units were 200 at this time. After a second course of 5 fevcr sessions combined with bismarscn, and followed by subsequent iodobismitol therapy (19 injections), the serologic reactions became negative and have remained negative for the past 5 years.

Secondary manifestations occurring between the first and second years of disease.—All of the cight patients who exhibited late secondary manifestations of syphilis (occurring between the first and second years of the disease) had failed to respond to previous chemotherapy. Hence, the patients in this group represented serious treatment problems. During the usual course

of chemotherapy such secondary manifestations as macular or macus lopapular eruptions, mucous patches, nasal vestibulitis, or recurrent ulcerat the site of the primary lesions had developed in these patients; two patients also had concomitant periostitis. All had strongly positive blood serologic reactions.

Four of these refractory patients responded both clinically and serologically to the combined therapeutic program. Three patients were improved following the usual course but did not attain serologic negativity or complete clinical remission until they had received additional fever-chemotherapy. Included in this group is another patient in whom severe generalized exfoliative dermatitis developed following the administration of arsphenamine. Because of this patient's marked idiosyncrasy to arsenic, no chemotherapy was combined with the first four fever treatments. The exfoliative lesions disappeared after the third fever treatment. Before the fifth fever treatment was given the patient was tested with a 1/1000-gram dose of neoarsphenamine. Two days later exfoliation again developed. At the beginning of the fifth fever treatment when the rectal temperature first reached 105° F. (40.6° C.), a similar quantity (1/1000 gram) of neoarsphenamine was injected intravenously. This injection was not followed by exfoliative dermatitis. During succeeding fever sessions, 0.1 gram injections of bismarsen were given when the rectal temperature reached 105° F. (40.6° C.); exfoliation did not occur. Because of this patient's extreme sensitiveness to arsenic when it was given without the protective action of fever, the usual follow-up course of chemotherapy was omitted. Despite the small total quantity of arsenic given in combination with artificial fever, this patient's serologic reactions, strongly positive before fever therapy was instituted, were reversed to negative and have remained so for 5 years.

In this connection, it is pertinent to record that none of our syphilitic patients has developed exfoliative dermatitis when the arsenical compound was employed concomitantly with artificial-fever therapy.

POSSIBLE INTENSIFICATION OF SHORT-TERM CHEMICAL TREATMENT OF EARLY SYPHILIS WITH ARTIFICIAL FEVER

Encouraged by the foregoing observations and by the remarkable researches of Chargin, Leifer, and Hyman (*31*) on the "5-day" massive-dose chemotherapy of early syphilis by the intravenous drip method, we have engaged in an investigation to determine whether or not it may be possible to abolish the disease in 1 day by combining a large dose of mapharsen with a single 10-hour fever session. One objection to the 5-day intravenous drip method is the significant proportion of arsenical sensitization reactions. It should be noted, however, that the toxic effects produced by mapharsen in the last series of cases reported by Hyman and his asso-

ciates were remarkably less than those produced by neoarsphenamine in the series of patients treated previously by this method.

Since we have noted consistently that an individual's tolerance to arsenic is definitely increased during fever, the possibility suggested itself of eliminating or of diminishing the toxic chemical reactions by combining massive chemotherapy with artificial fever and at the same time to retain, and perhaps to fortify, its therapeutic effectiveness.

The present plan of treatment is as follows: A 10-hour session of fever at 106° F. (41.1° C.) has been adopted tentatively as the initial unit of fever since these limits have proved to be safe and practical in the management of patients with refractory gonococcic infection. Prior to the fever session a single injection of 4 grains of insoluble bismuth is administered intramuscularly. During the first 8 hours of the height of fever, 180 milligrams of mapharsen are administered intravenously in divided doses by the "multiple syringe" method. No additional antisyphilitic therapy is given. Studies are now in progress to determine the minimum amounts of chemotherapy and of fever therapy required for eradication of the disease.

While no conclusions are permissible since the period of posttherapy observation is as yet less than 2 years, the prompt resolution of clinical symptoms and the favorable serologic responses would indicate that further diligent inquiry is demanded. The results of this purely experimental undertaking will be made the subject of a later report.

DISCUSSION

THE FACTS speak for themselves. Artificial-fever therapy has come of age in the thirteenth year since its birth. The magnificent work in malarial therapy, initiated by Wagner-Jauregg and adopted and expanded by capable workers in many lands, provided the stimulus which caused others to search for less hazardous ways of achieving a similar goal.

Indulgence in controversy as to the relative merits of one or the other method of producing therapeutic fever should be ended. Each has its place in modern therapeutics. Malarial therapy is cheaper, if no account is taken of the cost of continued hospitalization and the loss of income to those who can be treated with artificial-fever therapy without interruption of gainful employment. The cost of the apparatus for artificial-fever therapy is not high if the low cost per treatment is considered. The new types of apparatus are designed to give continuous service for many years.

Malarial therapy has some advantages in the management of large numbers of patients congregated in understaffed, underequipped institutions for the mentally sick, but it is to be hoped that most neurosyphilitic patients in the future will be treated prophylactically or during the early manifestations of paresis. Thus the necessity for the admission of such patients to hospitals for the insane will be eliminated. It is significant that artificial-fever therapy has now replaced malarial therapy in many outstanding psychopathic hospitals. In isolated communities and in hospitals not yet equipped for artificial-fever therapy, malarial therapy should be employed.

The persistent claim that the malaria plasmodium exerts a specific beneficent influence in cases of neurosyphilis, apart from the production of fever, has little justification in the light of the developments of the past decade. Regardless of whether biologic, chemical, or physical agencies are employed for the production of therapeutic fever, the results are entirely comparable. There is little room for further doubt as to the direct relationship between the height and duration of fever and the clinical results.

It is well known that malaria plasmodia provoke marked reticuloendothelial stimulation, with an activation of phagocytic clasmatocytes, probably, in part at least, as a result of the destruction of red blood cells by the malaria plasmodia. It has been assumed by some workers that the clasmatocyte assists in some obscure way in the destruction of Spirochaeta pallida. The thoroughgoing hematologic studies by Doan, Hargraves, and Kester (*32*) revealed that artificial fever causes a tremendous increase in the numbers of clasmatocytes, particularly in the lymph nodes, spleen, and

liver. Granulopoietic stimulation is much greater with artificial-fever therapy than with malarial therapy. In one of Doan's patients who was first treated with malaria a temporary leukocytosis of from 14,000 to 15,000 per cubic millimeter occurred after each chill. Following subsequent artificial-fever treatments in the hypertherm, a transient leukocytosis as high as 40,000 to 60,000 per cubic millimeter occurred. To quote Doan: "Artificial hyperthermia by physical means not only provides the thermal factor of importance for the inactivation of the Treponema pallidum and the gonococcus, but has now been demonstrated to exert a profound effect upon the cellular equilibria of the body—in the directions which we believe, at the present time, to be the most effective in the mobilization of the defense forces of the body against these diseases." Here again, the uniformity of clinical results when adequate fever is produced by either malaria or artificial fever argues against any specific action by the malaria plasmodium.

To administer either therapeutic malaria or artificial-fever therapy requires training and skill. The best results with either method are achieved by those who exercise the greatest diligence and care. It is a common observation that the death rate from malaria has declined from year to year as the workers in a clinic become more experienced in erecting safeguards against treatment complications.

Much more important than the type of apparatus selected for the administration of artificial-fever therapy is the skill and devotion of the physicians and nurse-technicians who engage in this specialized work. Essentially similar results have been obtained by scores of workers employing a wide variety of physical modalities. The important considerations are: First, the adequate preliminary training of those who are to accept the responsibility for the selection and for the treatment of patients requiring fever therapy; second, the selection of apparatus with which the treatments may be carried out with safety and with relative comfort to the patient.

SUMMARY AND CONCLUSIONS

1. AFTER A DECADE of rich and constantly enlarging experience with physically induced artificial-fever therapy, the successful results achieved by many workers in many lands are sufficiently comparable to justify the categoric statement that artificial-fever therapy is at least as effective as malarial therapy in the management of symptomatic or asymptomatic neurosyphilis. In the hands of many reliable investigators artificial-fever therapy has yielded significantly superior results. Patients who have not responded well to malarial therapy have been benefited by subsequent artificial-fever therapy.

2. There is unmistakable evidence that the extent of clinical improvement in neurosyphilitic patients is related directly to the height and the duration of fever. The thoroughly documented analyses made by statisticians of the United States Public Health Service provide proof that the clinical responses were distinctly inferior when relatively low temperature levels were employed. There is no longer any valid reason to assume that the malarial plasmodium exerts any specific effect upon Spirochaeta pallida.

3. Several investigators who have had long experience with malarial therapy and with artificial-fever therapy have abandoned malarial therapy in favor of artificial-fever therapy. This decision was determined largely by the observations that (a) patients tolerate artificial-fever therapy more readily, (b) a high proportion of neurosyphilitic patients can be treated with artificial fever on an ambulatory basis without interruption of gainful employment, and (c) treatment complications are minimized with artificial-fever therapy.

4. Since continuous hospitalization is not a requirement for treatment with artificial fever of most neurosyphilitic patients, the cost of the treatment is not necessarily greater than with malarial therapy. If the patient remains at his regular employment during the course of artificial-fever therapy, the cost is usually much less.

5. The employment of auxiliary chemotherapy in conjunction with any type of fever therapy is an essential requirement. There is evidence that the concurrent use of chemotherapy with artificial-fever therapy increases the therapeutic effectiveness of both agencies.

6. The hazards inherent in the various physical modalities used for the production of artificial fever during the first few years of the undertaking have been largely eliminated. Recognition of the physiologic changes produced by fever has led to the utilization of means to combat such effects.

A procedure which was looked upon as a technical feat a decade ago may now be applied by skilled workers with a frequency which approaches routine.

7. Developments of the past few years have demonstrated that equally favorable clinical and serologic results may be obtained with fewer total hours of artificial-fever therapy, applied in shorter individual sessions at more frequent intervals. This practice permits the treatment of more patients at less cost.

8. The excellent results following the use of combined fever-chemotherapy in cases of asymptomatic neurosyphilis indicate that the patient's best interests are served by the prompt administration of this form of treatment.

9. The exudative forms of ocular syphilis, in contrast to the degenerative lesions, usually respond promptly and favorably to combined artificial fever-chemotherapy. Procrastination should be avoided in administering fever therapy in cases of exudative ocular syphilis in which chemotherapy is ineffective. There is reason to believe that primary optic atrophy may sometimes be improved or arrested by fever-chemotherapy.

10. The addition of artificial-fever therapy to the program of chemotherapy will produce serologic reversal in the majority of patients with resistant seropositive latent syphilis.

11. The general recognition of the inadequacies of present-day chemotherapeutic programs in the management of early syphilis has led to investigations of the possible usefulness of artificial-fever therapy combined with chemotherapy in such cases. There is a growing body of evidence which indicates that artificial fever intensifies and fortifies the effectiveness of antisyphilitic chemical compounds. It seems possible that the time, effort, and expense required for the eradication of early syphilis may be lessened as the result of future researches in this direction. At the present time such methods of treatment should be considered strictly experimental. The results achieved thus far, however, should stimulate other investigators to engage in long-term, controlled experiments with a view to the introduction of more rapid, more certain, less dangerous, and less costly methods of treatment.

12. In the hands of skilled and devoted workers, artificial-fever therapy provides the venereologist with a potent therapeutic weapon.

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THE PRINCIPLES OF VENEREAL DISEASE CONTROL

A Detailed Discussion of the Recommendations for a Venereal Disease Control Program in State and Local Health Departments, as Outlined in the Revised Report of the Advisory Committee to the United States Public Health Service.

Nels A. Nelson, M. D., Baltimore, Md.

In collaboration with

Assistant Surgeon General R. A. Vonderlehr, Chairman
United States Public Health Service

Herman N. Bundesen, M. D., Chicago, Ill.

Joseph Earle Moore, M. D., Baltimore, Md.

William F. Snow, M. D., New York, N. Y.

Percy S. Pelouze, M. D., Philadelphia, Pa.

John H. Stokes, M. D., Philadelphia, Pa.

Udo J. Wile, M. D., Ann Arbor, Mich.

Lida J. Usilton, M. A., United States Public Health Service

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UNITED STATES PUBLIC HEALTH SERVICE

Thomas Parran, *Surgeon General*

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THE PRINCIPLES OF
Venereal Disease Control

A Detailed Discussion of the Recommendations for a Venereal Disease Control Program in State and Local Health Departments, as Outlined in the Revised Report of the Advisory Committee to the United States Public Health Service, 1941 [1]

INTRODUCTION

FIVE YEARS have passed since the enactment of the Social Security Act and the appropriation of funds by the Federal Government for the development of more effective public health work in the United States. Although the public responded enthusiastically to Surgeon General Parran's plea that we stamp out syphilis (*1*), actual progress in the development of the venereal disease control program was at first slow because the limited funds available had to be apportioned among the many activities of a general public health program. It was not until the enactment, by the Congress, of the Venereal Disease Control Act on May 24, 1938, that sufficient funds were made available so that serious consideration might be given to the specific problem of venereal disease control. These new funds, plus those made available through State and local appropriations, have made it possible to lay the foundation of a venereal disease control program in every State in the Union.

Evaluation of serologic tests for syphilis and investigations of the reliability of such tests have been undertaken and have been established on a permanent basis for all State laboratories. Studies of the efficiency of serologic test performance in municipal and private laboratories is under way in most States, as a result of legislative stimulation or of simple persuasion. Drugs for the treatment of both gonorrhea and syphilis are being distributed on a more general and more generous basis than ever before. Clinic service is being extended everywhere in populous areas, and much is being learned concerning how treatment may be provided in rural areas.

Personnel is being trained, and public education is going on apace.

[1] J. A. M. A., 116: 2585–2589, June 7, 1941

It is no longer impossible to discuss the venereal diseases in the public press or over the air. The medical literature is filled with information on the management of gonorrhea and syphilis, and the control of the venereal diseases has been accepted, everywhere, as a legitimate and a respectable public health problem.

In 1937, the first of the sulfonamides made its appearance. Interest in the control of gonorrhea had already been stimulated by research in fever and hormone therapy, by improvements in the culture of the gonococcus, and by the work of the American Neisserian Medical Society. Since gonococcal infection is one of the conditions which respond to the new chemotherapy, a great many investigators from almost every branch of the medical and allied sciences have been attracted to the study of this disease in the course of their investigation of the drugs. There is now great promise for the eventual control of gonorrhea.

In view of the progress which has been made since the first report of this Committee was published, early in 1936 (*2*), it now seems desirable to reconsider the earlier recommendations. Improvements and new developments in both treatment and control methods, the greater availability of funds, and the stipulation by Congress, in 1940, that the increase in Federal appropriation be used for the control of gonorrhea, make necessary some revision and a general broadening of the principles upon which health departments should build their venereal disease control programs.

The revised report of the Committee is divided into two parts. The first, in which only broad recommendations are made, has been published separately (*3*), but serves as the foundation upon which this second part has been built. In this second part an attempt has been made to outline a a complete program, in considerable detail, toward the establishment of which we believe that every State and other political subdivision of 500,000 population or over, should constantly strive. This program is based, first, upon the requirements of the United States Public Health Service in relation to the allocation of Federal funds and, second, upon all of those services which provide for reasonably adequate diagnostic, treatment, case-holding, case-finding, and educational programs.

It is well appreciated that the form of public health organization varies greatly from State to State, and that the part which any particular local agency should play in the execution of control programs cannot be prescribed in such a document as this. How the principles and procedures here described will be applied must depend upon local conditions. It is well appreciated, also, that both funds and basic facilities (such as general hospitals, transportation facilities, etc.) may be inadequate in many areas for the development of a full program. In those cases it should be the objective of the health department to make maximum use of existing facilities for the development of the program to the greatest possible extent,

having it constantly in mind that adequate diagnostic, treatment, case-holding and case-finding services are of first importance, particularly where communicable or potentially communicable infections are concerned.

ORGANIZATION OF THE PROGRAM IN COOPERATION WITH MEDICAL AND ALLIED PROFESSIONS AND LAY ORGANIZATIONS

In the organization of a venereal disease control program, careful attention should be given to the part to be played by the medical and allied professions and lay organizations. A health department cannot hope to develop an effective program without their active support and full participation. Although the health department must determine the scope and define the content of the program and administer many of the details, the private practitioner, the local and State medical societies, the hospital, nursing, welfare and voluntary public health agencies, the public schools, medical schools, and a variety of other agencies will have specific duties to perform in the actual application of many of the control procedures. Unless they are informed as to the health department's plan and are in general sympathy with its principles, they will either fail to assist to the full extent of their capacities or, in ignorance of the aims of the control program, may work at cross-purposes to the eventual detriment of the public welfare.

Interested, active, and well-informed lay organizations can be of invaluable assistance in securing public support for the program, and in extending the health department's channels of public information and education. It is doubtless to the disadvantage of many public health programs that not enough attention is paid to this matter of public relations.

State and Local Advisory Committees

In order to provide for representation of these cooperating agencies in the health department's plan and to promote good public relations, State and local advisory committees should be organized, whose function it should be to assist in the coordination of the venereal disease control activities of the corresponding health departments and the cooperating agencies. Local committees should be represented, as far as practicable, upon the State advisory committee in order that conflict may be avoided in the development of policies, and in order that local programs may keep pace with the State program.

To utilize further the resources of the community, when highly specialized problems arise, particularly of a technical nature, special advisory committees should be called together for temporary service, membership of which should include experts in the field in which the problem is located. Or,

this function may be assumed by subcommittees of the general advisory committee, which subcommittees should be permitted to invite nonmember experts to deliberate with them.

ADMINISTRATION OF THE PROGRAM

A Division of Venereal Disease Control

Venercal disease control should be the function of a separate division in the health department. Where that is impossible, or impracticable, it should be thc function of a subdivision, with a high degree of autonomy, in the division of communicable disease control or its equivalent.

Direction by a Venereal Disease Control Officer

Whether there is a division or a subdivision of venereal disease control, the program should bc directed by a venereal disease control officer who gives his entire time to the duties of his office, who is adequately trained in the administration of a venereal disease control program, and who is qualified for this office as recommended by the Surgeon Gencral of the United States Public Health Service after conference with the State and Territorial health officers[2].

The duties of the venereal disease control officer should include at least the following:

1. A dcfinition of the aims, purposes, and policies of the venereal disease control program. In consultation with the advisory committee, and as authorized by the State health officer, he should determine the scope of the venereal disease control program and define its content. Obviously, since it will be his responsibility to carry out the program, he should administer that part of it with which the division of vcnereal disease control is directly involved; that is, hc should have administrative supervision of all of the work of the division and over all of its personnel.
2. The collection and analysis of morbidity data. It is important that the venereal disease control officer keep himself informed, through the study of statistics, as to the results of the program and as to any progress which is being made toward the control of the venereal diseases. The actual collection and analysis of all morbidity data are the function of a division of vital statistics in some health departments. In such cases, however, the venercal disease control officer should be permitted to prescribe the data to be collcctcd for his purposes, and the scope of their analyses. He should have the fullest coopcration of the division of vital statistics in the planning and conduct of special studies, particularly as they

[2] See Appendix I. Qualifications of Personnel.

pertain to analyses of treatment, case-finding and case-holding performance of clinics and other treatment sources.

3. The establishment of effective cooperation with physicians in private practice, through conferences with State and local medical societies, provision of consultation services, distribution of effective and helpful medical literature, provision of laboratory services, distribution of drugs, and such other assistance as will lead to the willing participation of physicians in the health department's program.
4. The development of cordial relations not only with the public but with special scientific groups. He should conduct a continuous campaign of sound public education in venereal disease control. He should be the liaison officer between the health department and the several agencies which will share in the development of the program, working especially through the advisory committees, whether general or special, State or local. He should keep informed as to the findings of such agencies as the Cooperative Clinical Groups in both syphilis and gonorrhea, the Subcommittee on Venereal Diseases of the National Research Council, the Committee on Evaluation of Serodiagnostic Tests for Syphilis, and the American Neisserian Medical Society, and should report those findings to the local agencies interested in them.
5. Administrative consultation to other units within the health department such as the divisions of laboratories, maternal and child health, industrial hygiene. He should have a considerable voice in the determination of what emphasis is to be placed upon those parts of the program which may be administered by these other divisions in order that one service may not overbalance the other, and in order that one division may not work at cross-purposes with another, to the embarrassment of both and to the confusion of the public. He should consult with and give advice to local health departments over program development, administration, and balance. In this function he should act through the division of local health administration if there is one in the health department.
6. The organization and supervision of venereal disease clinics.
7. The organization and supervision of epidemiologic and follow-up services for clinics and private physicians.
8. Study and control of the efficiency of venereal disease clinics in terms of contact-tracing, efficacious treatment, and case-holding.

Auxiliary Personnel in the Division of Venereal Disease Control

The venereal disease control officer should be supported by such administrative assistants, professional consultants, case-holding and case-finding

personnel, and clerical staff as the execution of the program determined upon may demand. To whatever extent the program can be expanded from time to time, more nearly to approach the ideal, the staff of the division should be increased to permit the effective execution of the expanded program.

THE VENEREAL DISEASE CONTROL PROGRAM

Collection and Analysis of Morbidity Data

Provision should be made for the collection and analysis of morbidity data. Morbidity report forms should be simple and request only such data as may be exactly supplied with a minimum demand upon the physician's time and patience and as have actual statistical value. They should be provided by the State, for the sake of uniformity, and should be distributed and collected without expense to the physician. This may be accomplished through the use of some such medium as the business reply envelope or, if the form is issued in cooperation with the United States Public Health Service, the penalty mailing privilege may be used. All reports pertaining to venereal disease should be mailed in sealed envelopes, never on open post cards.

The morbidity report form should provide for the collection of the following minimal information:

MORBIDITY REPORT (FIGURE 1)

Date of report.
Name of patient (if required by law), or serial number if desired.
Address of patient (if required by law), or name if community of residence only.
Age or birth date, color, sex, and marital status of patient.
Diagnosis—[3]
Syphilis.
I. Acquired.
A. Early.
1. Primary.
a. Dark-field (positive) (negative).
b. Blood (positive) (negative) (doubtful).
2. Secondary.
3. Latent (less than 4 years' duration).
B. Late.
1. Symptomatic.
2. Latent (more than 4 years' duration).
C. Latent (duration unknown).

[3] See Appendix II. U. S. Public Health Service Nomenclature for Syphilis.

II. Congenital.
A. Manifestations (specify).

Gonorrhea (clinical) (smear positive) (culture positive).
A. Genitourinary.
B. Eye.
C. Other.

Chancroid.
Granuloma inguinale.
Lymphogranuloma venereum.
Signature and address of reporting source.

This morbidity report form will satisfy the requirements of the mechanical system devised by the United States Public Health Service and as applied in central tabulating units.

No special report of premature discontinuance of treatment is required by the mechanical system for lapses in treatment are recorded as provided for in the routine reports of progress made to the central tabulating unit. If the mechanical system is not used (or for the collection of reports from treating agencies not included in the mechanical system) a notice of premature discontinuance of treatment will be required. It should provide for the collection of the following minimal information:

REPORT OF DISCONTINUANCE OF TREATMENT (FIGURE 2)

Date of report.
Name and address of patient.
Age, sex, color, and marital status of patient.
Diagnosis (as on morbidity report) and date of that diagnosis.
If gonorrhea or early syphilis—
1. Duration of infection, or date of infection.
2. Amount of treatment given.

Signature and address of reporting source.

The epidemiologic report (report of contacts) should contain the following minimal information:

EPIDEMIOLOGIC REPORT (REPORT OF CONTACTS) (FIGURE 2)

Date of report.
Name and address of contact.
Age, sex, color, and marital status of contact.
Relation of contact to patient (husband, wife, paramour, etc.).
Diagnosis in patient (as on morbidity report).
If *patient* has gonorrhea or early syphilis, date of exposure to *contact*.
Signature and address of reporting source.

FIGURE 1.—SUGGESTED MORBIDITY REPORT FORM.

V. D. MORBIDITY REPORT — STATE OF _____

Name (if required by law), or Serial Number, if desired

Address (if required by law), or name of community only

Reason for admission to treatment:
- ☐ Selectec examinations
- ☐ Patient suspected venereal disease
- ☐ Routine medical examination
- ☐ Contact tracing
- ☐ Premarital blood testing
- ☐ Prenatal blood testing
- ☐ Other (specify) _____

- ☐ Male
- ☐ Female

- ☐ White
- ☐ Colored

- ☐ Single
- ☐ Married
- ☐ Widowed
- ☐ Divorced
- ☐ Separated

Age _____
or Birth date _____

ACQUIRED SYPHILIS

Early (under 4 years)
- ☐ Primary
  - ☐ Darkfield positive
  - ☐ Blood test positive
- ☐ Secondary
- ☐ Latent

Late (over 4 years)
- ☐ Symptomatic
- ☐ Latent

Latent
- ☐ Duration unknown

CONGENITAL SYPHILIS

- ☐ Form _____

GONOCOCCAL INFECTION

- ☐ Genitourinary
- ☐ Eye
- ☐ Other _____
  - ☐ Clinical
  - ☐ Smear positive
  - ☐ Culture positive

- ☐ CHANCROID
- ☐ GRANULOMA INGUINALE
- ☐ LYMPHOGRANULOMA VENEREUM

Previous treatment for this infection?

☐ Yes ☐ No

Signed _____ M. D.

Street (or institution) _____

City _____ County _____

Date _____ 19__

DETACH AND MAIL TO PATIENT'S PREVIOUS PHYSICIAN

To _____ M. D.

Address _____

Sir: Date _____ 19__

Name of patient _____

Address of patient (Street) _____

City _____ County _____ State _____
who has been under your care for:

- ☐ Gonorrhea
- ☐ Syphilis
- ☐ Chancroid
- ☐ Granuloma inguinale
- ☐ Lymphogranuloma venercum

is now under my care. I would appreciate a summary of the patient's medical record, including a statement of the nature and amount of treatment the patient has had.

Signed _____ M. D.

Address (Street) _____

City _____ County _____ State _____

FIGURE 2.—REVERSE OF MORBIDITY REPORT FORM.

A. Report of Lapse of Treatment. B. Report of Contact.

A ☐ REPORT OF LAPSE OF TREATMENT

Name (Patient) _____

Street _____

City _____ County _____

☐ Male
☐ Female

☐ White
☐ Colored

☐ Single
☐ Married
☐ Widowed
☐ Divorced
☐ Separated

Age _____

Total Treatment to Date—
([1] Dx*)

Drug:	Doses
Arsenical	------
Bismuth	------
Mercury	------
Tryparsamide	------
Other	------
Sulfonamide	------

Date of Last Visit

_____ 19__

Signed _____ M. D.

Street _____

City _____ County _____

Date _____ 19

B ☐ REPORT OF A PATIENT'S CONTACT

Name (Contact) _____

Street _____

City _____ County _____

State _____

☐ Male
☐ Female

☐ White
☐ Colored

Age _____
or
Birth Date
_____

☐ Single
☐ Married
☐ Widowed
☐ Divorced
☐ Separated

If [1] Dx*: Date of Exposure

_____

Relation to Patient

☐ Husband ☐ Son
☐ Wife ☐ Daughter
☐ Paramour ☐ Sibling
☐ Prostitute

Signed _____ M. D.

Street _____

City _____ County _____

Date _____ 19__

Use separate form for each contact.

DIAGNOSIS

Date of This Diagnosis

_____ 19__

SYPHILIS ACQUIRED

Early; under 4 years.
*☐ Primary
*☐ Secondary
*☐ Latent
Late; over 4 years.
☐ Symptomatic
☐ Latent
Latent
☐ Duration unknown

CONGENITAL SYPHILIS

☐ Form _____

*GONOCOCCAL INFECTION
☐ Genitourinary
☐ Other

Form _____

☐ CHANCROID
☐ GRANULOMA INGUINALE
☐ LYMPHOGRANULOMA VENEREUM

DIAGNOSIS IN PATIENT

Date of This Diagnosis

_____ 19__

SYPHILIS—ACQUIRED

Early; under 4 years.
*☐ Primary
*☐ Secondary
*☐ Latent
Late; over 4 years.
☐ Symptomatic
☐ Latent
Latent
☐ Duration unknown

CONGENITAL SYPHILIS

☐ Form _____

*GONOCOCCAL INFECTION
☐ Genitourinary
☐ Other

Form _____

☐ CHANCROID
☐ GRANULOMA INGUINALE
☐ LYMPHOGRANULOMA VENEREUM

[1] If diagnosis is marked with asterisk.

The mechanical system requires that all contacts shall be reported to the central tabulating unit. Where the mechanical system is not used, or for those treating agencies not included in the mechanical system, epidemiologic reports may be required, or their content modified, according to the following schemes:

1. If the name and address of every contact is required by law, use the form as outlined in every case.
2. If the name and address of every contact is not required by law, use the form as outlined but require the *name* and *address* of only those contacts who are not followed by the treating agency, or in whose follow-up the treating agency has failed.
3. Require reports only of those contacts who are not followed by the treating agency, or in whose follow-up the treating agency has failed, i. e., do not require reports of contacts followed successfully by the treating agency.

Requests for any additional data on any of these forms should be considered very carefully as to the probability that they will be supplied accurately, uniformly, and regularly; that they will not annoy or seriously inconvenience the physician or alarm the patient; and that they will supply really useful information.

It is convenient to provide space for all three reports (morbidity, premature discontinuance of treatment, and epidemiology) on a single form. This makes the issuance of more than one form unnecessary, which is important in that the reporting sources do not have to keep supplies of several different forms on hand. The single form may be used for any one of the three purposes. (See figures 1 and 2.)

ANALYSIS OF MORBIDITY DATA

Analysis of morbidity data should be provided for, either through the mechanical system or some simpler punching and sorting system. Potential duplication of reports may be detected by taking note of whether the patient has, or has not, had previous treatment for this infection; it being assumed that a patient who has had previous treatment has been reported previously. If the mechanical system is used, duplicates are automatically detected by comparisons of identifying data.

The aim of the ordinary analysis of morbidity reports is to determine:

1. The relation of the infection to the sex, age, color, and marital status of the patient.
2. The proportion of fresh infections, particularly with syphilis, to the total infections in all stages by sex, age-group, color, and marital status.
3. The source of the report and the probable influence of potential duplication of report upon the apparent quality of the problem.

4. The extent of migration from the community of residence for treatment elsewhere.
5. The rates of reporting in different areas and the relation of those rates to population differences, availability of clinic and other treatment services, and the cooperation of the medical profession.

Reports of premature discontinuance of treatment serve the dual purpose of enabling, or requiring, the treating agency to call for the assistance of the health officer in case-control, and of enabling the health officer to estimate, roughly, the case-holding ability of the treating agencies.

Reports of contacts permit the health officer to function in case-finding when the treating agency, for one reason or another, is inadequate to the situation. They also enable him to estimate, roughly, the case-finding efficiency of the treating agencies.

Since only a fraction of the fresh infections with gonorrhea or syphilis which actually occur come to medical attention early, and since reporting is notoriously incomplete, morbidity reports should be used only as a partial and minimal indication of the prevalence and incidence of venereal disease.

They must be used with caution even to estimate the distribution of infection in the population according to age, sex, marital status, or color, or as any measure of the proportion of fresh infections to total infections among persons seeking treatment. They should not be depended upon to measure the extent of the problem in the population; that can be approximately determined only by appropriate surveys of representative groups of the population of the area under consideration.

Examination of morbidity data from year to year, even in the same State, discloses that there are many related factors, other than those of decreasing or increasing incidence of infection, to account for the remarkable fluctuations in the number of case reports. Such factors as the availability and accessibility of treatment facilities, the varying interest of physicians, and the fluctuations in popular interest and understanding of the venereal diseases, will account for increases or decreases in the number of case reports. So, also, will new concentrations of population (as in Army cantonment areas) or changes in its composition, changes of personnel (and attitudes) in clinics, and the availability of funds for venereal disease control purposes.

The cross-checking of laboratory reports against morbidity reports may help to determine the completeness of morbidity reporting, but laboratory reports should not be considered as case reports. Laboratory findings are of assistance in making a diagnosis, but the diagnosis itself must be made by the physician, not by the laboratory. The attempt to integrate the two systems of reporting invariably leads to confusion, annoyance, and the improper use of both.

Analyses of the data derived from morbidity reports should be published

at regular intervals, in readily assimilated or interpreted form for the information of the public and, particularly, for the information of those medical agencies which make the reports.

In the larger venereal disease control units, at least, one or more epidemiologists should be employed to direct the collection and analysis of morbidity data, to make special studies, and to prepare material for publication. If funds are available and the volume of work warrants, a trained statistician should be employed to direct the technical preparation of statistical analyses; otherwise the epidemiologist should seek the advice and assistance of the statistician in the division of vital statistics or its equivalent.

Special Studies

Special studies of certain population groups should be made as an aid in determining the proportion of the population infected with venereal disease. Such studies made at given intervals may prove helpful in establishing possible trends and in pointing out special needs for the control of venereal disease in specific population groups. Studies might include inmates of mental and penal institutions, workers in industry, patients in prenatal clinics, and men tested under the Selective Training and Service Act. In studying the selected population groups, it is highly important to employ proper statistical safeguards, especially with reference to the age, color, and sex composition of the group. The limit to which results of studies on selected population groups can be applied to the total problem must be recognized, inasmuch as such selected population groups are rarely mutually exclusive or representative samples of the whole population.

Successful random sampling of the general population of the United States to determine prevalence, incidence, and trend has not been accomplished. However, through well-planned mass blood-testing programs, some fairly satisfactory indications of the extent of the infection in a given area have been obtained.

Mortality Data

It would be worth while if those health departments which can afford to do so would experiment with the confidential death certificate, in order that somewhat more accurate information may be obtained as to death rates from the venereal diseases. It is quite possible, of course, that the greater error in the mortality statistics for venereal disease arises out of failure to make the diagnosis of venereal infection as the cause of death, rather than out of its deliberate concealment by a false death certificate.

Laboratory Services

Adequate and universally available laboratory facilities for dark-field examinations and serologic tests for syphilis, and for microscopic examina-

tions for the gonococcus, are essential for the control of these diseases. Culture of the gonococcus is essential to a desirably high efficiency in the diagnosis of gonococcal infection and to controlled determination of cure.

Laboratory service should be offered without charge to any licensed physician or other medical agency, without certification of the patient's indigency. The practice in some places of requiring such certification of indigency is to be deplored. If the physician is required to make the certification, an unjustifiable expenditure of his time is necessary to ascertain the patient's financial status. If it is required of the patient, he is subjected to needless humiliation because of his unfortunate economic situation.

There should be at least a central State laboratory, supported by as many branch laboratories as the demand for serologic service may require. The possibility should be borne in mind that, under certain circumstances, approved private laboratories may be subsidized to advantage for the performance of laboratory work, but the subsidy should not exceed the cost of doing the same work in the State laboratory or in a comparable branch of the State laboratory.

LABORATORY REPORT FORMS

Laboratory report forms should be provided by the State and should uniformly contain the following items, as a minimum, regardless of format:

1. Date of collection of specimen.
2. Identification of patient. Full name or initials, address, age or birth date, sex, color, marital status. If the specimen was sent from a clinic or hospital the patient's case number should be included.
3. Identification of reporting source. Name and address of physician if a private practitioner; or name and official designation of physician submitting specimen for clinic or other treatment institution; indicating, also, the name and address of such clinic or institution.
4. Reason for submitting specimen. Blood serologic test for syphilis, dark-field examination, spinal fluid examination, gonococcus smear, gonococcus culture, gonococcus complement fixation test, or test for other venereal diseases (Frei, skin test for chancroid, Donovan bodies, etc., depending upon the services offered by the laboratory).
5. Purpose of test. Diagnostic first test, diagnostic repeat test, treatment control, premarital, prenatal, food-handler, serologic survey, Selective Service, etc.
6. Result of test. Laboratory specimen number. Recorded results of test in terms of positive, negative, doubtful, not done. Date of test, signature and official designation of person responsible for report-test result. Name and location of laboratory.

If the funds available permit only of the performance of a single test, that test should be used which has the highest degree of sensitivity and which can be performed to produce results with that degree of specificity which is currently prescribed by the Committee on Evaluation of Serodiagnostic Tests for Syphilis. When funds and program balance permit, the addition of a second test should be considered. In the selection of the second test, consideration should be given to one which, on evaluation, has proved most likely to produce positive results in specimens which produce negative results with the test already in use, provided, of course, that both tests are acceptably specific.

All laboratories should be required to use the terms "positive," "negative," and "doubtful" in reporting the results of serodiagnostic tests; and all report forms should bear, prominently displayed, a statement to the effect that a single positive test, in the absence of history or clinical evidence of syphilis, must not be accepted as final; and that a single negative test, in the presence of a history or clinical evidence of syphilis must not be accepted as indicating freedom from infection. A "doubtful" test should always be repeated if the test is being used as an aid in making a diagnosis or in the determination of serologic cure.

Supersensitive, so-called "screen tests," may be employed in the manner which their name indicates, i. e., as screen tests only. Their results should be reported to the physician only when negative. In that case it may be safely assumed that less sensitive tests will also be negative. When screen tests alone are positive, the question of technical false positive results cannot be ruled out. When, on the contrary, the positive result of the screen test is supported by the positive result of less sensitive tests, the report of the screen test result is unnecessary.

Studies of efficiency of serologic test performance.—State laboratories participate regularly in studies of the proficiency of performance by the Committee on Evaluation of Serodiagnostic Tests for Syphilis and are content with no lower standard of efficiency than that of the control laboratory which performs the same test. For local laboratories, whether public or private, a system of licensure or approval should now be set up under which regular evaluation of their serologic service should be made. No laboratory which cannot perform a test which conforms with current standards should be permitted to serve the public.

State laboratories should collaborate with the United States Public Health Service in the evaluation of local laboratories in order that a reasonable degree of uniformity may be attained in serologic laboratory service throughout the United States. At present there is too much variation in results and too little confidence in one State in the performance of serologic

laboratories in another State. When local laboratories are approved by a State laboratory which, in turn, has been approved by the United States Public Health Service, such laboratories should have interstate recognition.[4]

Standards for serologic laboratory performance.[5]—

1. Before either modifications of tests or new tests are adopted for general use they should be subjected to evaluation by an acceptable agency.
2. In those laboratories in which limitations of funds, personnel and equipment do not permit the pursuit of serologic research, the technical procedures described by the originators of reliable serologic tests should be followed in every detail * * * the serologist who experiences any difficulty in the performance of a test should communicate with the originator and endeavor to locate the source of the difficulty.
3. It is imperative that obsolete methods be abandoned.
4. Strict adherence to the originator's technic will not produce good results if an antigen is used which is not properly standardized * * * When antigen is purchased it should be secured from sources known to be dependable. Each new supply of antigen prepared in the laboratory should be standardized against a product secured from the originator * * * or from an equally reliable source.
5. It is essential that the persons who perform the tests should be thoroughly conversant with the principles of the reactions, the properties of the reagents, their preparation and titration, and the many possible sources of error or variation inherent in the technic * * * and have immediate access to one who is thoroughly qualified by training and experience to detect and correct the various sources of error affecting the reliability of the results.
6. Another source of difficulty arises when changes in personnel occur in the serologic laboratory. It is not uncommon to encounter false positive or false negative results or an excessive proportion of doubtful reactions following substitutions of personnel because of illness or vacation periods * * * if all workers are trained to adhere strictly to conventional technic, and if the laboratory director

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[4] The Conference of State and Territorial Health Officers, in 1941, through its Committee on Venereal Disease Control, reported that "it is the expressed opinion of the Committee on Evaluation of Serodiagnostic Tests for Syphilis that an entirely satisfactory level of efficiency in the conduct of serologic tests has been attained by practically all State laboratories and that such laboratories may be depended upon to supply a finding which is considered accurate within the limitations of the methods which are at present in general use." The Conference therefore recommended that "full reciprocity be extended by the States in the matter of acceptance of premarital serologic reports in all instances in which the procedure is not specifically interdicted by the wording of the various statutes." Following this recommendation, a number of States have announced that they will accept the reports of any State laboratory in connection with blood-test legislation.

[5] Abstract of reports of (1) committee on the need for adherence to conventional technics in the performance of reliable serologic tests for syphilis; (2) committee on improvement of methods for determining the efficiency of serologic test performance; (3) committee on minimal educational and training qualifications for laboratory directors and technicians and; (4) committee on licensing or approval. Published in the Proceedings Assembly of Laboratory Directors and Serologists, Hot Springs National Park. Supplement No. 9 to Venereal Disease Information, Washington, 1939.

exercises unusual vigilance at such times, the likelihood of such errors is greatly lessened.

7. The performance of tests by persons whose time is crowded with many other laboratory duties is fraught with hazard, since frequent interruptions make it impossible to give the required attention to every technical detail.

In the evaluation of local laboratories:

1. The State laboratory, or the laboratory which is to serve as a control laboratory, should have attained a satisfactory standard of efficiency in the performance of serodiagnostic tests for syphilis.
2. The evaluation of the local laboratory should follow in general the procedure of the Committee for the Evaluation of Serodiagnostic Tests for Syphilis.
3. The number of specimens from nonsyphilitic donors and from syphilitic donors should not be less than 100 for each group.
4. Syphilitic donors should be selected by a competent syphilologist and completely documented, and they should be so selected that not more than 10 percent of the positives should contain large amounts of reagin.
5. Because of the difficulty in obtaining large quantities of blood, not more than 30 laboratories should be included in any one evaluation.
6. Whole blood specimens are preferable for distribution since conditions should simulate those in ordinary practice, and the specimens should be mailed on the day of collection, after a firm clot has formed at room temperature. If there is to be any delay, the specimens should be refrigerated.
7. To qualify as satisfactory a laboratory should attain a sensitivity rating not more than 10 percent below that of the State control laboratory and a specificity rating of not less than 99 percent.
8. Laboratories once approved should be reexamined at least once every two years unless administrative changes indicate the need for an earlier examination. Opportunity for retesting should be offered more frequently to those laboratories which fail to gain a satisfactory rating.

For the approval or licensure of local laboratories:

1. When the United States Public Health Service is satisfied with the facilities offered by a State laboratory, approval, but not necessarily licensure of local laboratories should be undertaken by the State. In cities to which State sanitary codes or similar legislation do not apply, if the municipal laboratory has been found to be efficient, the municipality should undertake the supervision of its own local laboratories.
2. Federal funds should be withheld from State or local laboratories which perform inefficient tests for syphilis, and may be withheld, entirely, from any State which does not fulfill its laboratory obligations.

State health departments should discourage, either through publicity or legislation, the performance of serologic tests for syphilis by physicians in their private offices, or by small laboratories which are not subject to control.

Quantitative tests.—Provision may be made for the performance of a quantitative test in special cases, on specific request, when the diagnosis may be in question without it (as in serologically positive newborn infants). Quantitative tests have no routine diagnostic value, however, and they usually serve only to confuse the physician.

Serologic aids to the diagnosis of gonorrhea have not yet been developed to that point of efficiency and reliability which warrants their use for routine purposes.

BACTERIOLOGY

Dark-field examination.—State and local health department laboratories should be equipped for direct dark-field examination, provided personnel trained in its effective use is available. Every public venereal disease clinic should eventually be equipped for direct dark-field examination, but only as rapidly as clinic physicians or technicians can be trained in the recognition of Spirochaeta pallida.

The advisability of offering indirect dark-field service should be considered where direct dark-field service is not available. This method of sending specimens of chancre serum to a central laboratory in special, capillary-tube outfits, is urgently needed in many parts of the country where direct dark-field examination is not available. Although this method has not yet been demonstrated on an extensive scale to be a practical procedure, it should be studied further because of its potential value to practitioners in rural areas and because of the scarcity of physicians and technicians trained and experienced in direct dark-field technic.

Smears and cultures for gonococcal infection.—Every State and local health department laboratory should be equipped for the examination of smears from suspected cases of gonorrhea. Only a Gram stain [6] or an accepted modification thereof should be used.

Single-stain methods, employing one stain (such as methylene blue) are entirely unreliable and should not be employed. Every clinic at which gonococcal infections are treated should be equipped for the examination of smears stained by the method of Gram.

It should be made very clear, however, to all who use this laboratory procedure that it is often inadequate and frequently erroneous. Negative smears, by themselves, have no significance. "Positive" smears from vulvovaginal infections in children should carry no more weight than to prompt further investigation by culture, or, lacking cultural facilities, a thorough investigation of the child's sexual contacts and evidence that exposure to a known gonococcal infection probably has occurred. Even in the adult female, a single "positive" smear may have no significance unless supported by clinical evidence of infection and a history of exposure to a known infection.

Until the sulfonamides have been further investigated it should be as-

[6] See APPENDIX III. Diagnosis of Gonococcal Infection by the Microscopic Examination of Films Stained by Gram's Method.

sumed, on the basis of evidence now available, that smears are useless as criteria of cure if these drugs have been administered.

Cultures must be made, or sexual control by abstinence or condom should be applied, for at least 2 months after symptomatic cure has been attained.

Wherever adequate bacteriologic laboratory service is now available in relation to clinic service, culture of the gonococcus should be undertaken. Technicians should have special training under the supervision of bacteriologists experienced in gonococcus culture. Culture service should be extended as rapidly as possible to all clinics where gonococcal infections are treated, as an aid to diagnosis and determination of cure.

Distribution of Drugs

for the treatment of syphilis

At least two of the common arsenical preparations (one to be an arsenoxide), and at least one generally accepted bismuth preparation,[7] should be distributed without cost to physicians and all other medical agencies authorized by law to administer drugs in the treatment of syphilis.

If tryparsamide is to be distributed for the treatment of central nervous system syphilis, the physician to whom the drug is distributed should be warned [8] of the precautions to be taken in its use.

for the treatment of gonococcal infection

Sulfanilamide should not be used in the treatment of gonococcal infections. It produces serious reactions which introduce an unnecessary element of risk or discourage regular taking of the drug by the patient. It produces asymptomatic carriers of the gonococcus who may remain carriers of infection for many months. Sulfapyridine cures a higher proportion of cases but it, too, causes many serious reactions. Since an equally effective and less toxic drug (in the dosage used in the treatment of gonococcal infection), sulfathiazole, is now available, there should be no occasion for the use of sulfapyridine in the treatment of this disease. Purchased in quantity, by the State department of health, it is relatively very inexpensive considering its efficiency. Newer drugs should not be used routinely until their therapeutic efficiency and their safety have been determined by competent evaluation, which should include cultural determination of cure.

Treatment Services

general principles

The provision of adequate public treatment services is a basic principle of venereal disease control. It is a matter of readily verified fact that most

[7] The most widely used and generally accepted bismuth preparation is bismuth subsalicylate suspended in peanut or olive oil, each cubic centimeter of the preparation containing 0.13 gm. (2 grains) of metallic bismuth.

[8] See Appendix IV. Memorandum Concerning the Use of Tryparsamide.

of the infected who seek treatment at public clinics are either on relief or are managing a precarious independent existence. Many are young people with small earning capacities if they have any work at all. The treatment of the venereal diseases, and especially of syphilis, is time consuming and, at private practitioners' rates, is expensive. Those of the infected who can afford long continued medical care at the hands of private physicians will not often be found in public clinics, where the danger of recognition is great, where long periods of waiting are the rule, where mass methods may leave little room for close patient-physician relationships, and where a multitude of other embarrassments and inconveniences must too often be tolerated.

The venereal diseases are communicable diseases. The right of the community to protect itself against exposure to communicable disease is recognized wherever there is civilization. In providing public treatment for the indigent infected with venereal disease, the community exercises a prerogative consistent with this right to protect itself. It is only in the public clinic that the large mass of the economically handicapped can be given efficient service at a price which the community can afford to pay. The provision of adequate treatment is vastly more than the simple introduction of medication into the patient. Consultation, case-holding and case-finding services are important functions of venereal disease control which could hardly be provided for the great number of the medically indigent in any other way than through organized clinic services.

In making provision for treatment in public clinics, the health department should first survey the resources of the community. It should determine how much clinic service is already available in private or public hospital out-patient departments or in other polyclinics. It should determine whether there are hospitals which do not have venereal disease clinics but which could contribute effectively to the more adequate service of the community by the addition of such clinics. It should determine whether, if all of the actual and potential hospital services are utilized, additional ad hoc clinics, to be operated by the health department, will be needed, and where they should be established to serve most effectively the area under consideration.

Having surveyed the needs of the area and having determined what services are actually and potentially available, the health department should hold conferences with the local medical society and the hospitals, under the auspices of the advisory committee, at which the needs of the community should be outlined, the available services identified, and a statement made as to the extent to which the health department can assist, financially and in consultation, in the development of an adequate treatment program.

This drawing together into a cooperative plan of the various public

and private agencies for the treatment of the venereal diseases will be a major demand upon the tact, breadth of vision, and generalship of the venereal disease control officer. It should be as much an objective of his campaign to win the enthusiastic cooperation and acceptance of modern standards from hospitals and groups which feel no need for public funds, and little desire to accept public guidance, as to purchase such cooperation from clinics and groups eager to supply it in exchange for State funds for equipment and personnel. The successful operation of even these latter groups and clinics depends as much upon the earned confidence of the medical profession, the hospital superintendent, and the clinic in the venereal disease control officer and his program, as they do upon the financial factor of control of personnel and practice.

DEFINITION OF BENEFICIARY OF PUBLIC CLINIC SERVICE

Diagnostic and treatment facilities should be provided for:

1. The diagnosis and emergency treatment of all persons who apply.
2. All patients referred by private physicians either for continued treatment or for consultation.
3. All patients unable to pay for private medical care.

If a patient asks to be referred to a private physician or is found upon investigation to be able to pay for private medical care, he should be referred to his own physician if he has one, after diagnosis and emergency treatment if necessary. If he has no private physician, he should be supplied with a list of physicians known to the clinic as available and qualified to treat venereal disease.

Determination of ability to pay for private medical care should be the responsibility of the treating agency, subject to health department approval of policy in those clinics which are maintained from public funds. The practice which has been followed in some places of admitting only those patients to the clinic who have been referred by private physicians should be abandoned. The private physician is not always the best arbiter of who should be entitled to a public service. Patients who cannot afford private medical care should not be forced to apply to private physicians for entree to a public clinic.

State and local health departments should publish widely, for the public benefit, the procedure to be followed by patients who need medical attention for venereal disease. In doing so, however, they should neither urge nor advise any person to apply to a public clinic, even for a blood test, if he is able to pay a physician. If a person appears at a clinic of his own volition, or having been referred by a physician, he should be admitted for diagnosis and emergency treatment as prescribed above (see 1.); but the public should not be urged, without any economic qualification, to flock

to public clinics. The public should not be encouraged to believe that a blood test is adequate in itself; a proper examination for syphilis includes a carefully taken history and an adequate physical examination.

No patient who is referred by a physician, or who is admitted to the clinic only for a diagnosis, should be told the result of a blood test or the findings on examination. He should be referred to his physician, to whom the information should be sent, for a report. The physician or the medical agency who is to be responsible for the care of the patient should be permitted to interpret the results of physical examination or laboratory studies to the patient.

Clinics supported wholly or in part by Federal funds should admit patients from adjoining States or other parts of the country. Transients, temporarily within the area of service of any clinic, should be admitted regardless of the source of clinic funds. If place of occupation, or other valid consideration, makes it more convenient or reasonable that a patient attend a clinic outside the area of his residence, he should be admitted to the more reasonably available clinic.

DEFINITION OF PHYSICAL QUALITY OF CLINIC SERVICE

Clinics should be so located as to be easy of access and of maximum convenience to the population of the areas which they are to serve. The number of clinic sessions should be such as to meet the needs of the area without overcrowding or unreasonable delay. Night sessions should be held in sufficient numbers and at such hours as to prevent loss of time from work to employed patients. Special attention should be paid to special conditions such as advanced pregnancy, the need of a patient to catch a train, to return to work, or to return to children left at home.

Clinics should be held in clean, well-lighted, well-ventilated rooms, so located and arranged as to offer adequate privacy but not to imply isolation (as of communicable disease), nor segregation (as of undesirable people). The physical arrangements should be such as to insure privacy in history-taking, physical examination and treatment, to provide adequate waiting-room and toilet facilities, and to contribute to the self-respect of the patient. In other words, the accessibility and the physical character of the clinic should be such as to invite and encourage regularity of attendance; not to discourage it or to imply that any treatment at all, no matter how disreputable the environment in which it is administered, is good enough for the venereally infected.

Children are preferably handled in a family clinic with late afternoon or Saturday morning hours. Their mothers should be treated for their venereal infections during these same sessions, and prenatal and pediatric care when necessary should also be available in these family clinics.

CLINIC PERSONNEL

All clinic personnel should be technically equal to the particular functions which they must perform.

Minimal clinic personnel should consist of (a) a qualified physician who is a graduate of a recognized medical school, who has completed at least 1 year of general hospital internship, who has had at least 6 months of special training, under supervision, in the management of the venereal diseases, and who has a tactful and sympathetic personality and a particular interest in the venereal diseases and their relation to the public health; (b) a qualified technical nurse who should assist the physician in the technical aspects of clinic operation, the routing of patients through the clinic, the entry of clinical notes of a routine nature, etc.; and (c) a clerk who should keep clinic records and statistics, attend to the clerical aspects of the follow-up system, and attend to the clinic correspondence. To this fixed minimum of intramural personnel there should be added such assistants in all of the categories as may be necessary to the efficient and effective operation of the clinic without undue waste of the patients' time, and such case-holding and case-finding personnel as may be adequate to the problem with which the clinic is confronted. (See "Case-finding and Case-holding," page 48.)

CLINIC EQUIPMENT

Clinic equipment should be adequate to the proper and efficient handling of the patient, his adequate physical examination, and his competent treatment. Tables should be available so that patients may be given intravenous and intramuscular injections lying down, although it is permissible to give intravenous treatments to a patient sitting in a chair. Neither form of treatment should be given to a patient standing up, since serious accidents may occur if the patient faints, or jumps.

Adequate facilities should be available for the collection of specimens for examination in the laboratory and in the clinic for the immediate examination of smears, chancre serum (by dark-field), urine, unless adequate laboratory service is available close at hand.

If the clinic is a part of a well-developed out-patient department of a hospital or part of a well-developed polyclinic, the venereal disease clinic itself need not be equipped for the more complicated special examinations such as gynecologic, urologic, neurologic, ophthalmologic. If, however, these special consultation services are not directly available, and the clinic medical personnel is not trained to make these examinations, provision should be made for referring the patient to special consultants in the community or to some adequately equipped consultation clinic elsewhere for examination. This is absolutely essential if tryparsamide is to be administered in the treatment of neurosyphilis, since ophthalmologic examinations must first be made.

History, physical examination and treatment record.—Clinic records should provide for recording the patient's medical history, the results of an adequate physical examination, the results of laboratory examinations and physical progress examinations, treatments given, reactions to treatment, tests for cure, and the condition of the patient at the time of any interruption of his connection with the clinic whether because of cure, no further need for treatment, transfer to treatment elsewhere, or unauthorized discontinuance of treatment. The record should provide, further, for recording the identity of all of the patient's contacts and the result of their follow-up.

Case-holding records.—I. THE MECHANICAL SYSTEM: When it is properly based upon accurate diagnoses and accurate and adequate progress data, the mechanical system provides clinic directors with a record-keeping device that facilitates effective case-holding. This system was developed as the result of studies of case-holding power in venereal disease clinics, which revealed that ineffective case-holding coincided with inadequate record keeping. Complete and accurate case records in a form which permits rapid tabulation and analysis, and accessible without delay to the clinician and administrator, are essential to efficient clinic performance from the administrative, treatment, and case-holding viewpoints. A system by which the mass of data could be reviewed quickly, economically, and currently would be of the greatest advantage. The mechanical system is an attempt to provide such a device.

In order to adapt the machine system to the recording of data for venereal diseases, it is necessary to obtain an inventory of the active cases already under treatment and to set up a central tabulating unit to punch all cards and process the data. Thereafter, the procedure used in securing the required information for the continuance of the system and the preparation of the reports consists in maintaining an up-to-date record of every service rendered the patient.

The treatment source furnishes the health department a copy of the standard report form on each new admission for a venereal disease. This record gives all the information required in the central tabulating unit to set up the master or summary card for the new patient.

Summary punch cards are used upon which all of this basic data may be recorded for any one of the venereal diseases, and the record is kept current by means of a punch card known as a progress card. The treatment source, by means of the progress card, notifies the central tabulating unit each time a service is rendered the patient. The progress card is punched in the central tabulating unit and machine-filed with the summary card for the corresponding case. At desired intervals the data on the progress and summary cards are added together by machine, the new summary card

being automatically punched to carry forward the accumulated history.

The data on the summary punch card in the central tabulating unit is, therefore, actually a duplicate of the data in the patient's clinic case-record, but it is in a form which lends itself to rapid evaluation either of the patient's progress and status or of the performance of the entire clinic service.

II. The Tickler System: Unless the mechanical system is used as an aid to case-holding, an efficient tickler system should be used. This system makes use of an appointment calendar.

At the time of the patient's first visit, he is given an appointment for his next visit. The date of this appointment is entered on the patient's record and is checked in the proper space on the tickler card by means of half an X, thus /. The tickler card is then inserted in a date file behind the date upon which the next visit is to be made. If the patient appears on that date, the X is completed. If he does not appear, the tickler card is placed in the follow-up file, thus automatically starting the process.

If the patient appears before the date of his appointment, his record will indicate the date of the appointment and thus locate the tickler card in the date file. If he appears soon after the date of appointment, and before follow-up can be begun, the fact that the date of appointment has

Figure 3.—Tickler Card, 4 by 6 inches

[Different colors may be used for different diseases]

Name _____ Record Number _____
Address (City and Street) _____
Sex _____ Age _____ Color _____ Marital Status _____ Date Adm. _____

Date of Diagnosis	Diagnosis

19__	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	19__
Jan.																																Jan.
Feb.																																Feb.
Mar.																																Mar.
Apr.																																Apr.
May																																May
June																																June
July																																July
Aug.																																Aug.
Sept.																																Sept.
Oct.																																Oct.
Nov.																																Nov.
Dec.																																Dec.
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	

passed (as will be evident from his record) will indicate that the tickler card is in the follow-up file.

The follow-up file may be divided into sections, or the cards identified with colored tabs, to indicate which cases are in need of prompt and intensive follow-up (early syphilis, syphilis in pregnancy, etc.).

FIGURE 4.—FOLLOW-UP FORM, 4 BY 6 INCHES

[Face]

Name _____ Record Number _____
Address (City and Street) _____
Sex _____ Age _____ Color _____ Marital Status _____
Last diagnosis _____ and date _____

Patient's Reason for Lapse
- ☐ Financial
- ☐ Social
- ☐ Occupational
- ☐ Transportation
- ☐ Illness
- ☐ Ignorance of need for ℞
- ☐ Indifference
- ☐ Reaction to ℞
- ☐ Complaint against clinic

What? _____

☐ No reason obtained

Outcome of Follow-up
- ☐ Returned to this clinic
- ☐ Reported at other clinic
  Where? _____
- ☐ Reported to L. M. D.
  Who? _____
  Where? _____
- ☐ Could not be found
- ☐ Moved out of area
- ☐ Follow-up ineffective

Date last visit _____
Date missed app't. _____
Date refer to follow-up _____
Date follow-up closed _____
Elapsed time _____ weeks

[Reverse]

Follow-up Record			Letter	VISITS			
Date				Patient Seen	Patient Not Seen	Behalf of Patient	Name of Visitor
Mo.	Day	Yr.					
Totals							

Through the use of this system, it is possible by referring to the tickler cards in the date file to determine which patients are due at any given clinic session and to have their records ready before the patients appear.

FIGURE 5.—EPIDEMIOLOGY FORM, 4 BY 6 INCHES

[Face]

Name _____ Record Number _____

Address (City and Street) _____

Sex _____ Age _____ Color _____ Marital Status _____

Diagnosis in patient _____ and date _____

Name of patient _____ Record Number _____

This Contact Is The

- ☐ Father
- ☐ Mother
- ☐ Husband
- ☐ Wife
- ☐ Brother
- ☐ Sister
- ☐ Son
- ☐ Daughter
- ☐ Paramour
- ☐ _____

of the Patient

☐ Prostitute

Outcome of Epidemiology

- ☐ Contact reported to this clinic
- ☐ Contact reported to other clinic
  Where? _____
- ☐ Contact reported to L. M. D.
  Who? _____
  Where? _____
- ☐ Contact could not be found
- ☐ Contact has moved out of area
- ☐ Epidemiology ineffective

Date of diagnosis in patient _____

Date epidemiology completed _____

Total elapsed time _____ weeks

[Reverse]

Epidemiologic Record				VISITS			
Date			Letter	Contact Seen	Contact Not Seen	Behalf of Contact	Name of Visitor
Mo.	Day	Yr.					
Totals							

Any of these records which have not been used during the clinic session will immediately identify the patients who did not appear and who are potentially in need of follow-up. If faithfully used, this system provides a simple method through which case follow-up may be initiated promptly, and the attendance status of every patient may be constantly watched. If proper statistical summaries are kept at every clinic session, the efficiency of the clinic in case-holding can be determined with relative ease.

Epidemiologic record.—(Fig. 5).—Forms are necessary for procuring and recording epidemiologic data. As soon as a patient's contacts are identified, an epidemiologic record should be started and turned over to the clinic epidemiologist. When the investigation has been concluded, the completed form should be filed as a clinic record and preserved for subsequent analysis of the clinic's epidemiologic performance, the result of the investigation having first been entered upon the record of the patient who identified the contact.

If the mechanical system is used, it should be possible to determine currently how well the epidemiologic investigation of each contact is proceeding. On the other hand, the simple tickler system can be used for contacts as well as for patients. On the tickler card there may be entered by means of suitable symbols the dates upon which letters were written or visits made to the contact, as well as the dates of his subsequent visits to the clinic for examination. By dividing this tickler file into sections or by using colored tabs, it may be determined which contacts are in need of immediate and intensive epidemiologic investigation.

CLINIC FINANCES

The cost of clinic maintenance should be budgeted as accurately as possible on an annual basis. It should include reasonable remuneration of all personnel including the physicians, all cost of routine clinic maintenance, and of any contemplated improvements or additions to the service. The clinic should then be assured of an appropriation, or "subsidy," or reimbursement on some basis adequate to meet the total cost as set forth in the budget, whether or not fees are collected from patients. Those clinics, then, which do collect fees from semi-indigent patients should credit the fees collected to general income, by which amount the payments from tax funds may be decreased. Tax funds thus released may then be used for improvements in service or for the extension of services to other areas. Fees collected from patients should never be used for specific purposes such as the payment of physicians' salaries, nor should the quantity or quality of clinic service be dependent in any way upon such fees. If the quantity or quality of service to be rendered has to depend upon the collection of fees, they will vary according to the current ability of the patients to pay, or there will be a tendency to attempt to collect more than the

patients can afford and so lead to irregular attendance or premature discontinuance of treatment.

Clinic physicians and any other intramural, part-time personnel who serve only during the hours in which the clinic is in session should be paid per clinic session *attended;* never on a flat rate per month.

TYPES OF CLINICS

In hospital out-patient department.—Venereal disease clinics are likely to serve the public best, due to the greater privacy offered and the auxiliary services available, if they are maintained as functions of out-patient departments of general hospitals. Whether these are private or public (municipal, county, etc.) hospitals, the clinics should be administered by the hospitals in which they are located even though they may be partly or fully subsidized by the health department from tax funds. Clinic personnel should be employed and discharged by the hospital management and should be responsible to the hospital alone. The practice of placing health department personnel in clinics administered by other agencies is to be discouraged for it leads to division of authority and is destructive of discipline and esprit de corps. The venereal disease clinic should be as much the responsibility of the hospital, alone, as any other clinic in the out-patient department.

Under such an arrangement the hospital will retain its identity as a free agent, the health department will be relieved of complicated administrative duties, the working relationship between the hospital and the health department will not be disturbed by fear of official domination or upheavals in government, and the clinic staff will find it much easier to secure the cooperation of the auxiliary services in the out-patient department.

In whatever manner the health department may subsidize this form of service (whether on a cost-per-visit basis, or full subsidy, or in the provision of funds for the maintenance of some of the services) there should be close agreement between the health department and the agency which provides the service as to what constitutes satisfactory standards of service. Constant effort should then be made toward the attainment of those standards.

The advantage of having hospital beds available is so great that no venereal disease clinic in the out-patient department of a general hospital should be subsidized by the health department if the hospital refuses to admit patients with venereal disease to its beds.

In polyclinics not connected with hospitals.—Privately operated polyclinics should be invited to provide venereal disease clinic service on the same basis as hospitals with out-patient departments, but they should be required to demonstrate that they have access to an adequate number of hospital beds for those of their patients with venereal disease who may need hospital care.

In health department health centers.—Venereal disease clinics in health depart-

ment health centers should be considered only when it is impossible to serve an area adequately through clinics in out-patient departments or private polyclinics, unless the health center has general polyclinic equipment and provides for necessary consultation services and has suitable hospital connections.

If there are no hospital clinics, or if those which exist will not cooperate or are inadequate to the needs of the community, the health department clinic is the next best choice. Any necessary consultation services (ophthalmologic, neurologic, cardiovascular, urologic, gynecologic, roentgenologic,) should be provided for by the appointment of special consultants or by arrangement with the nearest polyclinic, so far as such consultation services exist, if at all, in the community.

If health department buildings are not available throughout the area to be served and a central clinic will not adequately meet the needs of the area, it is recommended that the plan which has been adopted in certain places be given consideration. In these places health center quarters have been built into the public schools by the departments of education for the use of the health department. Prenatal, child health, venereal disease, and other clinic services are offered in these school health centers. There may be a considerable advantage to the community in this association of health services with the public schools, where hospital out-patient services are not adequate or do not exist.

If a number of these centers are maintained in a given area, it may be of advantage to employ a full-time clinic staff which will move from center to center on different days. This would result in more uniform service and make it more possible to provide an adequately trained and experienced personnel.

In rural areas.—I. The Stationary Center and a Mobile Personnel: In the more populous rural areas, where conveniently located quarters can be found (as in empty stores, school buildings, churches) and where the population of the area is not scattered at too great a distance from the center, stationary treatment centers may be considered. These should provide general health services as well as treatment for the venereal diseases, and they may be served by a mobile personnel. Some arrangement should be made so that the county nurse or some local volunteer will have the equipment ready, water heated, the rooms warm, and other necessary preparations attended to before the clinic staff arrives, in order to save time.

Such centers however small, and although they may be used only once a week, may give rural populations the sense of having a permanent contact with the health department in the form of health services of their own. They could be used as the official quarters of the district or county nurses when they are in the area between visits of the clinic staffs.

II. The Mobile Clinic: When the population is so scattered that it is

more difficult to transport the patients to a permanent center than to transport the clinic to the patients, the mobile treatment unit has been demonstrated to be effective and economical in providing treatment and other health services. The personnel of a mobile clinic unit should consist of a minimum of one physician, one nurse, a chauffeur and, if possible, one clerk, and the clinic should be equipped to provide all of the diagnostic and treatment services which can be provided by any small ad hoc venereal disease clinic, plus prenatal examination, immunization against smallpox and diphtheria, and other simple health services, particularly for the control of communicable and preventable diseases.

Whether clinic service is provided in rural areas through the stationary center with a mobile personnel or through a fully mobile unit, neither type of service should be considered unless the area is within the jurisdiction of a well-organized county or other local health department and unless the clinic service is administratively controlled by the health officer.

TREATMENT SERVICE THROUGH PRIVATE PHYSICIANS

Where no form of public clinic service is practicable, private physicians may be paid for treating indigent patients. No completely satisfactory solution has yet been found for the problem of how to select the physicians who are to be paid for this service. If certain physicians are chosen, whether by the health department or the county medical society, those who have not been chosen sometimes refuse to cooperate in the matter of referring indigent patients to the designated physician. Physicians who are subsidized for the treatment of indigent patients should not be permitted to collect any part of the fee from those patients. The reimbursement of the physician should be a direct arrangement between him and the health department—not between the physician and the patient. Experience has demonstrated that there is a tendency to try to collect too much from the patient, with subsequent neglect of those who can pay nothing and irregularity of treatment on the part of those who can pay only now and then.

In areas not too distant from clinic service, a physician may be appointed to the clinic staff and may then treat patients in his area who are admitted to him *through the clinic*. He will use clinic record forms, clinic methods, clinic case-holding and case-finding services, and discharge the patients through the clinic. His office, in other words, becomes a room in the clinic, at the end of a long "corridor." He should be paid at the same rate as any clinic physician, per clinic session—a session to consist of a prescribed number of patients treated per week. He should attend the clinic at regular intervals, with reimbursement at clinic rates, and be available for clinic appointment in the event of a vacancy in the regular staff. In this way patients who are near enough to the clinic to report there for diagnosis, occasional check-ups and final discharge but too distant to attend

regularly, may be provided with routine treatment in the extramural clinic physician's office.

This method of providing treatment in not too rural arcas which arc not more than 15 or 20 miles from an established clinic, appears to bc working satisfactorily in certain places without objection from the medical profession in the area.

TREATMENT SERVICE FOR PREGNANT WOMEN

As a matter of general principle, pregnant women who require treatment for venereal disease should be given both prenatal care and treatment for their infections at the same clinic. If this is impossible, every effort should be made to hold sessions of the prenatal clinic and the venereal disease clinic at the same time so that the patient will not be obliged to make a separate trip on another day to one or the other clinic.

LIMITED TREATMENT SERVICES

If funds are inadequate for a treatment program to include all forms and stages of gonorrhea and syphilis, first attention should be given to gonorrhea, early syphilis, syphilis in prcgnancy, and congenital syphilis. Treatment of gonorrhea under such circumstances may be limited to the administration of sulfathiazole or its therapeutic equivalent or superior. Although neglect of those cases which do not respond to sulfonamide therapy is to be deplored, in principle, it is better to treat and cure a high proportion of cases than to neglect them all. It is a matter for the health department, however, to recognize its responsibility for those cases whieh do not respond to chemotherapy and to train its clinic physicians in their management, and so far as possible in the meantime, to refer all such cases elsewhere for treatment.

CONSULTATION CENTERS

When well-equipped hospital out-patient departments are only occasionally available, they should serve as centers to which patients may be referred by less well-equippped clinics for consultation, so far as geography and transportation facilities permit.

TRANSPORTATION AS A FUNCTION OF TREATMENT

It is recognized that it is a function of public treatment service to make it possible for those who need treatment to reach it. It often happens that patients who cannot afford medical care are also unable to pay for transportation to a public treatment center. Provision of adequate treatment for infection with venereal disease should be held to include, therefore, provision of transportation or the cost of transportation to those who would otherwise be unable to obtain treatment.

Provision of transportation, or the cost of transportation, should be arranged through the treating agency. Any complicated system which

requires that the patient be referred to the health department or to the welfare board serves only to discourage the patient and to promote irregularity of treatment. Transportation should be considered as much a part of treatment as any of the drugs used or any other part of the clinic service, to be administered like these others by the clinic.

TRANSIENT AND TRANSFERRED PATIENTS

In providing for transient and transferred patients, the original clinic should give all patients a statement of treatment received as a means for promoting continuity of therapy. If the patient is to be transferred to a known treating agency, a complete summary of the patient's record, including diagnosis, treatment, and condition at the time of transfer, should be forwarded to the new treating agency. The mechanical system for the collection of morbidity reports, as evolved by the United States Public Health Service, has been found to facilitate the exchange of information of this kind.

It is further advised that an effort be made to preserve the continuity of treatment of patients who desire to return to the care of their private physicians. This may be encouraged by the exchange of treatment data between the clinic and the physician. In fact, it should be invariably considered the duty of the clinic director to forward to the patient's physician an outline of the plan of treatment which the clinic director has in mind for the patient. Physicians should be informed, also, that the clinic medical service is always available for purposes of consultation at any time as the treatment of the patient progresses.

HOSPITAL SERVICES

Hospitalization should be provided, at the discretion of the clinic chief, for open early syphilis under certain circumstances, particularly in case of infectious relapse or for recalcitrant patients, or when there are unusual home or social conditions. It should also be provided for lumbar puncture if this service cannot properly be provided in the clinic, or when there are circumstances which make it advisable to have the patient under hospital control.

Hospital care should be provided for severe postlumbar puncture reactions, fever therapy for neurosyphilis, acute congenital syphilis in infants, some cases of acute interstitial keratitis when intensive local treatment is necessary, various forms of late visceral syphilis, acute gonococcal pelvic inflammatory disease, gonococcal vulvovaginitis in children from homes where there are other girls and home conditions are poor, gonococcal ophthalmia in any age group, gonococcal arthritis, and other acute complications of gonococcal infection, such as epididymitis, prostatic abscess, pelvic abscess.

If hospitals are lacking in the area, or within reasonable distance of the area, some form of medical and nursing service should be provided for the care of the patients at home, so far as any of these services can be administered at home.

Diagnosis, Treatment, and Determination of Cure in the Clinic

Unless the clinic is in charge of physicians trained and expert in the management of the venereal diseases, it would be well to prescribe the procedures to be followed for routine purposes. It should be definitely understood that consultation should be sought in any unusual case or in one which needs more expert attention or more complicated treatment than the clinic can provide.

GONORRHEA

Diagnosis.—I. In the Male: Cultural evidence of the presence of the gonococcus is adequate, in itself, for the diagnosis of a gonococcal infection. Cultural evidence is defined as including those fermentation tests which differentiate between the gonococcus and other members of the group of gram-negative diplococci which resemble the gonococcus.

According to the American Neisserian Medical Society, (*4*) a diagnosis of gonorrhea may also be made in the male, under the following three conditions:

1. If intracellular, gram-negative diplococci which resemble the gonococcus are found in smears from the male genito-urinary tract, if the history of the infection or the clinical evidence is presumptive of gonococcal infection.
2. If extracellular organisms are found in typical clusters during the earliest hours of an acute infection, and the history or clinical findings are presumptive of gonorrhea, a clinical diagnosis of gonorrhea may be made and the case treated as such. Smears should be made at frequent intervals thereafter as intracellular organisms may be found at a later date (especially in a case which does not respond to sulfonamide therapy).
3. A clinical diagnosis should be made in the presence of a suggestive history and suspicious clinical findings, confirmatory laboratory findings being lacking, and the patient treated as if he had gonorrhea. Repeated search should be made for the gonococcus thereafter, however.

If the diagnosis of gonorrhea has been made elsewhere, on the basis of evidence which would have been acceptable to the clinic if the patient had first been seen in the clinic, that diagnosis may be accepted and the patient treated for gonorrhea, if necessary, even though gonococci can no longer be found.

II. In the Female: The American Neisserian Medical Society recognizes the difficulty of obtaining laboratory confirmation of the diagnosis of gonorrhea in women, and makes the following recommendation (*5*): "Laboratory confirmation of diagnosis, whether by smear or culture, is relatively easy in acute infections in either male or female, although the diagnosis of gonorrhea in female children should always be supported with evidence of direct exposure to a known infection or cultural proof, including fermentation tests, that the gonococcus is present. In chronic infections in women, however, even repeated cultures may be negative, and, if the patient is to have the advantage of prompt treatment, the diagnosis will have to be made clinically if a history of exposure or of promiscuous sexual intercourse is obtained. On the other hand, a single positive smear from an adult female should be supported by clinical evidence of infection or a history of exposure to infection, before the diagnosis of gonorrhea is made."

Specimens for either smear or culture should be taken from the urethra after thorough massage of the para-urethral (Skene's) glands, and from the cervix after thorough cleansing of the vagina with dry gauze or cotton swabs and manipulation of the cervix between the blades of a bivalve speculum. Specimens collected from the urethra without prior massage of the para-urethral glands, or from the cervix without first cleansing the vagina and removing any cervical plug, will usually be highly contaminated with overgrowing organisms or contain no gonococci.

The patient's history should include an account of the symptoms which she has or has had, such as dysuria (not common), vaginal discharge, vulvar pruritis, pelvic inflammation (including abdominal surgery), Bartholin abscess or cyst, acute arthritis, and menstrual disturbances not otherwise adequately accounted for. It should further include any history of exposure to a known gonococcal infection, of sexual promiscuity, or of having infected another person with gonorrhea. The mother of an infant with gonococcal ophthalmia neonatorum, for instance, may usually be assumed to be the source of the infant's infection.

Treatment.—I. In the Male: Local treatment (irrigations, urethral injections, etc.) need not be used in any form except in patients resistant to chemotherapy as described below, or in some complications, and then only by specially trained personnel. Improperly given local treatment is quite likely to do more harm than good. The following plan of local treatment is, in general, that recommended for the Army and Navy by the Subcommittee on Venereal Disease of the National Research Council (*6*).

A. Anterior urethritis (as determined by history and two-glass urine test).

1. Irrigations with warm 1 :8,000 potassium permanganate solution: Daily (ideal) but adequate minimum 2 or 3 times a week. Reduce to one per week when discharge has almost disappeared

and continue until discharge has been absent 3 or 4 weeks and urine clear 2 or 3 weeks.

2. Urethral injections by the physician, following irrigation, of not more than 8 cc. of 5 percent mild silver proteinate (not more than 1 week old). Continue until symptoms and discharge disappear, and the urine is clear, although permanganate irrigations will be continued for 2 or 3 weeks longer.
3. Urethral injections by the patient, if he can be trusted after demonstration to use them properly. Injections, 2 or 3 times a day of not more than 8 cc. of mild silver proteinate, using a glass syringe of capacity not greater than the volume to be injected. Reduce to not more than 1 injection per day when the discharge has almost subsided. Discontinue when the discharge has stopped, and the urine is clear.

B. Posterior urethritis.

1. Stop all treatment at the onset of posterior urethritis, except for hot hip baths for relief of pain.
2. When the acute symptoms have subsided, resume the anterior urethral irrigations with 1:8,000 permanganate. After each irrigation, allow not more than 200 cc. to run into the bladder (but not enough to cause bladder discomfort) under not over 3½ feet of fluid pressure. Irrigate 2 or 3 times per week until prostatic massage is begun, then adjust irrigations to massage.
3. Under no circumstances should massage be begun in less than 4 to 6 weeks after the beginning of treatment. Pain, inflammation, frequency, dysuria, hematuria, and bladder discomfort should have been absent for 2 or 3 weeks. The urine should have been clear except for shreds or very slight haziness in the first glass. The bladder should be partly filled with urine or irrigant, which is to be voided after massage. Massage twice a week, reducing the number to once per week as the pus content of the secretion approaches normal (not over 3 to 5 cells per high power field). The average uncomplicated infection will require massage for from 3 to 6 months. Massage should never cause pain; if it does, or if it causes a return of the discharge, it should be discontinued temporarily.

C. Complications, such as epididymitis, prostatic abscess, arthritis, ophthalmia, must be treated by experts and often need hospital care. It may be possible to give at least early relief in epididymitis through the use of chemotherapy.

II. In the Female: Local treatment of gonorrhea in the female is, at best unsatisfactory. If the onset is very acute, external cleanliness and daily hip baths should be prescribed. When the acute stage has subsided, mildly

antiseptic, warm, daily douches may be prescribed. Topical applications are of no value. In acute pelvic inflammatory disease the patient should be given bed rest, ice bags or hot water bottles (whichever give the greatest comfort) to the lower abdomen, and long, hot douches. It is important that the bowels be kept open by the mildest effective laxative. Treatment should be continued until all clinical evidence of infection has subsided, after which the patient should be observed several months for relapse.

III. Chemotherapy in Both Male and Female: The American Neisserian Medical Society recently prepared a statement concerning the chemotherapy of gonorrhea which so well represents current expert opinion that it has been considered worth while to reproduce a considerable part of it here.

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THE SULFONAMIDES[9] *IN THE MANAGEMENT OF GONORRHEA (7)*

The American Neisserian Medical Society

(*June 3, 1941*)

Sulfanilamide.—Sulfanilamide should not be used in the treatment of gonococcal infection. Early reports of its high efficiency were commonly in error because of failure to evaluate cure by cultural methods. Immediate clinical response was good in a large number of cases, but subsequent clinical relapse was common, and cultural studies made by many later observers disclosed that innumerable asymptomatic carriers were being produced. These carriers remain potential spreaders of infection for many months.

Sulfapyridine.—Sulfapyridine cures a much higher proportion of cases, but it causes more serious reactions than sulfanilamide. Since a newer drug, sulfathiazole, is equally effective and causes few immediate reactions (in the dosage used for the treatment of gonorrhea), this should be, at present, the drug of choice.

Sulfathiazole.—There is much excellent evidence, based on careful and extensive cultural study, that sulfathiazole cures as high a proportion of gonococcal infections, in either sex, as any other sulfonamide now available. Of the failures, some do not respond at all, and the remainder either relapse or become asymptomatic carriers for variable periods.

Although many excellent treatment schemes have been and still are used, the following has the advantage of being simple and rapidly effective: 2 grams per day for 10 days.[10] The daily dose is usually divided into 4 doses of 0.5 gram (one pill) given every 4 hours.

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[9] The group of drugs generally known as the sulfonamides, which has appeared since the discovery of sulfanilamide, numbers several hundreds. Others are constantly appearing. Of those already discovered, only a very few have been used in the treatment of gonococcal infections. To date, only three of these, sulfanilamide, sulfapyridine, and sulfathiazole, have enjoyed wide use and have merited serious study. The American Neisserian Medical Society, in cooperation with the United States Public Health Service, has been engaged for 2 or 3 years in a continuous evaluation of the sulfonamides in the management of gonorrhea. This statement of the Society's opinion as to the place of the sulfonamides in the management of gonorrhea was adopted at Cleveland, Ohio, on June 3, 1941, at the Seventh Annual Meeting of the Society. Since the Neisserian Medical Society of Massachusetts was about to issue a somewhat similar statement, based upon its own experience, the two statements were combined and will appear in essentially identical language.

[10] Alternative dosage (recommended and used successfully by several competent observers)—4 grams per day for 5 days. (N. A. N.)

The daily dose for children is 0.5 grain per pound of body weight; but the total should not exceed 2 grams. The fluid intake should not be restricted.

In men, if there has been no clinical improvement by the fifth day, the drug should be discontinued for the time being, for its continued use will accomplish no favorable result. The clinical picture in women is so often confused by other conditions, however, that it is the rule to give the full course in every case and to depend upon bacteriologic study for proof of response.

Infections which fail to respond to one course of sulfathiazole may often be cured by a second course, similar to the first, following a rest period of a week or 10 days. More than two consecutive courses of the drug, however, are of questionable value. In definite drug failures, careful search should be made for the possible cause of failure, and recourse should be had to local treatment. In some cases, fever therapy may be indicated.

The patient should be kept under observation during the course of sulfathiazole therapy because reactions may occur as a result of the administration of any of the sulfonamides. If there is persistent vomiting, rash, or other severe reaction, the drug should be discontinued. Moderate nausea will be reported by an occasional patient, but is not ordinarily cause for stopping the drug. There is no need for determining blood levels when the recommended dose is used, for the concentration of the drug in the blood seems to have no relation to the clinical and bacteriologic result. Blood counts and hemoglobin determinations may be indicated for some patients.

Determination of cure.—When treatment has been concluded, the patient should be directed to abstain from unprotected sexual contacts for at least 3 months. Relapse should ordinarily occur within this period, if it is to occur. If cultural facilities are available cultures of prostatic secretion and urine sediments in the male and of exudates from the cervix and the para-urethral (Skene's) glands in the female should be made from four to six times during this period. Smears, also, should be examined, but negative smears should not be relied upon as evidence of cure. More than three to five pus cells per oil immersion field, in prostatic secretions, are significant of prostatic infection of some kind (not necessarily gonococcal), but freedom of prostatic secretion from pus is not evidence of cure of a gonococcal infection.

In some women who have gonorrhea, the vaginal discharge will continue, or reappear, after treatment has been stopped. It is worth while to search for other causes in these cases before concluding that the gonococcal infection has not been cured or that the patient has been reinfected.

Some valuable advantages to be gained.—It is of the greatest advantage to begin treatment of infections in women immediately, without waiting for laboratory confirmation of diagnosis, if the history of exposure or a known infection in the sexual partner in addition to clinical evidence in the patient points to gonococcal infection. Prompt treatment will usually prevent extension of the infection into the pelvic cavity or control it if it has already occured. The risk of permitting an infection to spread upward is much greater than the risk of using the drug in a case that may not be a gonococcal infection. Smears and if possible cultures, should be made at the first visit, however, since they may help to establish the diagnosis. Once treatment is begun they are likely to be negative.

Since sulfathiazole seems to cure a high proportion of gonococcal infections in both sexes, the prompt use of this drug should result in an early "chemical quarantine" of many of the infections. Every effort should be made, however, to keep the patient under sexual control for at least 3 months after apparent cure.

There is reason to be optimistic over the eventual control of gonorrhea for it should now be possible to cure it much faster than it can spread. The medical profession has at hand a medium through which, if properly used, one more dangerous and prevalent communicable disease may be added to those that were once serious public health problems.

Since determination of cure after chemotherapy has been discussed in the foregoing statement, it will be discussed only in relation to local therapy in the following section.

Determination of cure after local therapy.—I. In the Male. Tests for cure should never be attempted until there is every reason to believe that the infection is cured. Then calibration of the urethra by the passage of one or two well-lubricated sounds may be undertaken. If any resultant discharge contains more than a few pus cells or any gonococci, treatment must be resumed. The test should be repeated in from 4 to 6 weeks and the prostatic secretion examined 3 or 4 times thereafter at 2 to 3 week intervals. If no relapse occurs, the patient may be discharged as probably cured but should protect any sexual partner by using a good condom for several months thereafter. If culture service is available, the above tests for cure should be supported by culture of the prostatic secretion and urine sediment at two-week intervals for 2 or 3 months. Indulgence in alcohol or sexual excitement are NOT recommended for prescription as criteria of cure. If the patient does indulge in either against orders, however, the result should be considered with other criteria.

II. In The Female:

1. Examine clinically for evidence of infection, examination to include palpation of pelvic contents for tenderness or masses.
2. Examine smears, using the Gram stain, once every 2 weeks for 3 months, specimens to be taken from the well-massaged para-urethral (Skene's) glands, and from the cervical canal after all accumulated discharge has been completely wiped away and the cervix massaged between the blades of a bivalve speculum. *Do not use lubricant on speculum.*
3. If culture service is available, the above tests for cure should be supported by culture of specimens from the urethra (Skene's glands) and cervix once a month for 3 or 4 months.

SYPHILIS

Diagnosis.—I. Primary Syphilis: Moore (*8*) very briefly and ably states the "Diagnostic Maxims in Primary Syphilis" as follows:

1. Any genital sore in male or female is possible primary syphilis until proved to be otherwise.
2. Any indolent lesion anywhere on the body (especially lips, tonsils, fingers) which fails to heal in 2 weeks may be primary syphilis.
3. The diagnosis of primary syphilis is a laboratory, not a clinical procedure.
4. *Do not* treat suspected primary syphilis locally until repeated dark-fields are negative.

5. *Do not* give antisyphilitic treatment on suspicion; prove the diagnosis.
6. There is reason for urgent haste in diagnosis; *hours count!*

In the same publication, Moore outlines the diagnostic procedure as follows:

1. Dark-field of surface serum; if negative, repeat at least three times on consecutive days before local treatment.
2. If surface dark-field is negative, do dark-field of aspirated serum from lesion's base, or, dark-field of aspirated material from lymph node.
3. If you have no dark-field microscope, send the patient at once to someone who has; or send capillary tube specimen to nearest laboratory.
4. Do serologic test at first visit. If any of these tests are positive, treat at once. If all are negative—
5. Do serologic test follow-up for 3 months, weekly for first month, every 2 weeks thereafter.

No physician who has not actually had training and experience in the recognition of Spirochaeta pallida should attempt the diagnosis of syphilis by the dark field; too many serious errors are likely to be made. This is especially true of lesions in the mouth where organisms resembling Spirochaeta pallida are frequently found.

II. Secondary Syphilis: Moore's diagnostic maxims in secondary syphilis are as follows:

1. Do blood serologic follow-up (3 months) on any lesion which was possibly primary syphilis.
2. For any generalized skin eruption—DO A SEROLOGIC TEST.
3. For any sore mouth or throat which does not heal in 10 days—DO A SEROLOGIC TEST.
4. For any unexplained patchy loss of hair—DO A SEROLOGIC TEST.
5. For any iritis or neuroretinitis—DO A SEROLOGIC TEST.
6. For any vague bone pains or polyarticular arthralgia—"acute subacute, or chronic infectious arthritis"—DO A SEROLOGIC TEST.

It is highly desirable to recognize the approach of the open, infectious stage of secondary syphilis before it develops—hence, the serologic follow-up advised in maxim 1. The next five maxims call attention to the five common manifestations of secondary syphilis—generalized skin eruptions, mucosal lesions, alopecia, iritis and arthralgia, although others, much less common, do occur. Moore states that 95 percent of all patients with secondary syphilis will present one or a combination of these five mani-

festations. Unfortunately, the lesions of secondary syphilis may either be completely lacking or so trivial and evanescent as to be overlooked by patient and physician alike. Further, unless blood tests are made, the fact that the lesions are due to syphilis may be entirely missed, and some other diagnosis made.

Fortunately, the properly performed serologic test has its highest *negative* value during the secondary stage of syphilis. It is always positive (100 percent). If it is negative, there is practical assurance that the patient has some other disease. On the other hand, it must be remembered that a patient may have a positive blood test as the result of an old infection with syphilis, and at the same time have any one of the above signs or symptoms as the result of a concurrent condition, not syphilis. The history of exposure, the history of a primary lesion, or the therapeutic test may help to settle the question. Consultation with an expert may be necessary. Moore lists 40 skin diseases, 23 conditions of the mucous membrane of the mouth, 16 conditions of the mucous membranes of the genitalia, 4 causes of loss of hair, and 4 causes of iritis which may be confused clinically with the lesions of secondary syphilis. He prescribes the following, invariable procedure in all cases:

1. Suspect syphilis.
2. Examine immediately the skin and mucosae for other lesions of early syphilis.
3. Whether or not such lesions are present, do a blood serologic test at once—*every genital lesion in male or female is syphilitic until proved not to be.*

III. Latent Syphilis: All syphilitic infections are latent at some time, and most of the time until ultimate break-down occurs. *There is no way to recognize latent syphilis except by serologic tests.*

IV. Syphilis and Pregnancy: Few syphilitic pregnant women have lesions, and history and physical examination are nearly worthless as aids in making the diagnosis in this group. The diagnosis can be made in most cases only by serologic tests.

V. Congenital Syphilis: So many mothers with syphilis are receiving some treatment during pregnancy, or have had treatment before pregnancy, that outspoken clinical evidence of infantile congenital syphilis is becoming increasingly rare. The recognition of syphilis in the infant, therefore, is becoming more and more a laboratory problem. The steps to be taken toward making the diagnosis are as follows:

1. Suspect syphilis in every baby of a known syphilitic mother, whether or not she was treated before or during pregnancy.
2. Suspect syphilis in puny, ill-nourished, wizened infants who "won't gain," in infants with skin rashes of any type, in those with snuffles, or those with "pseudoparalysis."

3. In older children, suspect syphilis if there is "pink eye" (it may be interstitial keratitis), deafness unless clearly middle ear, hydrarthrosis of the knees (Clutton's joints), osteomyelitis, and peculiar second dentition. Check suspicion by serologic tests of both child and other members of its family.
4. If the facilities are available, make a dark-field examination of scrapings from the wall of the umbilical vein. The finding of Spirochaeta pallida establishes the diagnosis at the earliest possible moment.
5. If quantitative serologic tests can be made, do quantitative serologic tests on the cord blood and on the infant's blood at 1, 2, 4, 6, 8, and 12 weeks of life and at intervals thereafter for at least the first 2 years. If the child does not have syphilis, the titer will decrease and usually become negative before the end of 6 or 8 weeks. If the child has syphilis, the titer may rise, or it may fall at first and then rise.
6. If titration cannot be done, it may be assumed that a positive serologic test of the infant's blood after 6 weeks to 2 months means syphilis. If the test is negative at 2 months, it should be repeated at 6 months, 1 year, and 2 years. If all these tests remain negative, the child certainly has escaped infection with syphilis.
7. Roentgenograms of the infant's long bones at the age of 2 weeks may establish the diagnosis if there is characteristic evidence of syphilitic osteochondritis at the epiphyseal lines. Negative findings do not exclude the possibility of syphilis. Interpretation of the roentgenograms must be made by an experienced roentgenologist, since deposits of bismuth (if the mother has been treated with bismuth) may make differential diagnosis difficult.

VI. Late Syphilis: Late syphilis may attack any part of the body. Its manifestations are so numerous and its differential diagnosis so difficult, clinically, that it has well earned the name of "Great Imitator." It is impossible, outside of a voluminous textbook, to discuss the diagnosis of late syphilis adequately. Moore (*8*) has prepared an excellent summary of the more important points, to which the reader is referred. Here it must suffice to repeat a part of his summary:

> The average physician does not possess sufficient knowledge of all the medical specialties to permit him to recognize clinically all the varied manifestations of syphilis which may fall within these special domains. He can remedy this deficiency if he will—
>
> a. Keep constantly in mind the fact that syphilis is a prevalent disease.
> b. Remember to what extent syphilis may imitate or be imitated by many other diseases.
> c. Familiarize himself * * * with the names of those diseases causing most diagnostic confusion.
> d. Suspect syphilis when he is confronted with any of these diagnostic possibilities.
> e. Recall that modern serologic tests are 95 percent efficient in the diagnosis of untreated syphilis.
> f. Check his clinical suspicion by a serologic test of the blood.

Treatment.[11]—I. General Principles: In general, no treatment should be given until the diagnosis is made either by dark-field or confirmed serologic tests. No therapeutic tests should be used. If, under the pressure of a most unusual and extreme emergency, treatment for a lesion suspected of being a chancre must be begun before laboratory confirmation of the diagnosis can be obtained (or if treatment has been begun elsewhere without adequate diagnosis), such treatment should conform fully to the scheme for early syphilis and must be carried through to completion as if a positive diagnosis of syphilis had been made.

Treatment should be begun with an arsenical in early and latent syphilis but with bismuth in cardiovascular syphilis and certain forms of central nervous system syphilis. The preferred arsenical, outside of clinics with well-trained medical personnel, is arsenoxide (mapharsen). Under expert direction, arsphenamine or other arsenicals may be employed. The preferred bismuth preparation is bismuth subsalicylate in oil.

Tryparsamide and fever therapy should not be used except in well-equipped centers, under expert direction.

Each treatment should be recorded upon the patient's clinic record, including the date, form of drug, dose given, and any reaction. A record should be kept in the clinic of the name of the manufacturer of the drugs administered and the name, serial number and expiration date (if any) of the product used in each clinic session.

It cannot be too strongly emphasized that clocklike, calendar regularity of treatment without long or short variation or lapses, is critically important both to control of infectiousness and cure. It is most important in the first 12 months. Every effort should be made to impress this fact upon all of the clinic personnel on every occasion.

Emphasis should be placed upon the need for the completion, by each patient, of the full treatment schedule in the time called for by the type of infection which he presents. The results of serologic tests should not be permitted to interfere with this schedule of treatment. So-called "abortive" procedures should not be used in seronegative primary syphilis, and "treatment to noninfectiousness" only, should never be accepted as the objective of any clinic in any case.

The infectiousness of syphilis is not to be predicated upon the results of

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[11] This outline of treatment procedures and controls is a greatly condensed selection of material from several sources, including publications of the United States Public Health Service, reports of the Subcommittee on Venereal Diseases of the National Research Council, and notations by individual members of the Advisory Committee. It is intended only to serve as a rough guide to the health officer in his attempt to set up minimal standards of clinic performance. He should insist that every member of every clinic medical staff shall study, in detail, the original publications from which this material has been withdrawn.

blood tests but upon the total time, course, laboratory tests, physical inspection, and treatment summation of the case.

II. Treatment of Early Syphilis (Less Than 4 Years' Duration): Unless otherwise specifically authorized by an expert, treatment should be of the continuous-alternating type, i. e., without rest periods between courses, and with arsenical courses alternating with bismuth (not alternate or simultaneous injections of the two drugs except as indicated for overlap).

The maximum dose of mapharsen is 0.06 gram; of arsphenamine, 0.3 gram for women and 0.4 gram for men; of neoarsphenamine, 0.75 gram for women and 0.9 gram for men; and of bismuth subsalycilate, 0.2 gram (of metallic bismuth). An average course of arsenical consists of 8 (weekly) injections, and of bismuth, 10 (weekly) injections. Overlap may be provided for by lengthening the arsenical course to 10 or 12 (weekly) injections, and beginning the bismuth injections with the last 2 or 3 arsenical injections. The next course of arsenical may then be begun with the last 2 or 3 injections of the bismuth course. The ratio of total arsenical injections to bismuth injections during the course of 70 weeks of treatment should be about 30 arsenical to 40 bismuth. In the average case of early syphilis this will constitute adequate treatment (if the spinal fluid is negative) regardless of whether the blood tests remain positive (unless there has been a serologic relapse after an original reversal to negative).

III. Treatment of Late Latent Syphilis (More Than 4 Years' Duration): Here the aim of treatment is to increase the probability of "cure" or "arrest" and to decrease the probability of clinical relapse or progression over the probable result if no treatment were given. The continuous method of treatment is desirable but not absolutely essential. Rest periods probably do no harm. Maximum results are obtained with about 20 injections of an arsphenamine combined with large amounts of heavy metal, the latter administered over a long period of time. An outline of treatment which has proved satisfactory is as follows:

Weeks:
1–7—Arsenical, 8 weekly doses.
8–17—Bismuth, 8–10 weekly doses.
18–25—Arsenical, 8 weekly doses.
26–37—Bismuth, 12 weekly doses.
38–45—Arsenical, 8 weekly doses.
46–57—Bismuth, 12 weekly doses.
58–69—Rest period.
70–81—Bismuth, 12 weekly doses.
82–93—Rest period.
94–105—Bismuth, 12 weekly doses.

Assuming physical evidence of syphilis to be absent at original and recheck examinations and the spinal fluid to be normal, treatment may be

stopped at this point regardless of whether the blood serologic test is positive or negative.

IV. Serologic Observation During Treatment:

A. In primary and secondary syphilis—

Blood tests should be done:

1. At the beginning of treatment.
2. At the second visit if the first test is negative.
3. At the 16th week (average positive case will become seronegative).
4. At the 24th week (if positive, indicates need for spinal fluid examination).
5. At the beginning and end of each bismuth course thereafter.
6. Once in 3 months during 2 years' posttreatment observation.
7. Before discharge from the clinic at any time.

Spinal fluid examinations [12] should be done:

1. Between the 24th and 52d weeks in all cases.
2. If the fluid is abnormal, repeat at least once in 6 months.
3. If weekly or strongly positive blood tests result after the blood has once become negative. (Such a positive test should be promptly checked by repeat tests to rule out the occasional false positive before concluding that there has been a serologic relapse.)

B. In early latency (first 4 years of infection)—

Blood tests should be done as in primary and secondary syphilis.

C. In late latency (infections more than 4 years old).

Blood tests should be done every 3 months whether the patient is on treatment or probationary observation.

D. In all latent syphilis—

Spinal fluid examinations should be made:

1. Before, or as soon after, treatment is begun as practicable.
2. If, after a series of negative blood tests, the blood becomes positive as confirmed by prompt recheck.
3. Before discharge, if practicable, unless previously negative.

V. Control of Relapse and Infectiousness: Early syphilis should be regarded as openly infectious until the second dose of an arsenical has been given, and should be rated as potentially infectious if treatment, for any reason, is irregular or inadequate (subschedule). Patients should be warned to look for and report mouth, skin, and genital lesions, and physical

[12] See Appendix VI. Interpretation of Spinal Fluid Findings.

inspection of these areas should be made as often as circumstances permit, during treatment and at each posttreatment inspection. Dark-field examination is of great help in recognizing these relapse lesions; the blood test may be negative.

The involution of the chancre or secondary lesions should be watched to detect treatment-resistant cases. Inspect at least at 3d and 8th weeks after treatment was begun.

Infectious relapse or infectious cases which are treatment-resistant should be considered by an expert consultant for application of special treatment methods and quarantine control. They should not be discharged from observation without approval of the consultant, regardless of blood or other tests.

VI. Prevention and Detection of Reactions: A physical examination and an examination of the urine should precede the institution of treatment. Minimal medical inspection before each treatment should consist of the inspection of:

1. Face—for edema of eyelids and dermatitis.
2. Open mouth—for bleeding gums and petechiae.
3. Sclerae—for jaundice.
4. Elbow flexures, wrists—for dermatitis and petechiae.
5. Patient—for signs of intercurrent infection or fever.

The patient should be questioned something as follows: Sick after last treatment? Bowels loose? Stool black? Urine dark? Skin itch? Eyes bother? Any rash? Gums or nose bleed? Pain in arm or hip?

It is of the greatest importance that proper attention be paid to technic, particularly as it pertains to the preparation of drugs and solutions and their administration to the patient. It is also important to know what to do for the patient who has a reaction. [13]

Treatment should be stopped and the patient closely observed (hospitalized if necessary) if any of the following reactions occur:

1. Any itchy dermatitis of face and flexures.
2. Jaundice.
3. Petechial or other hemorrhagic lesions.
4. Evidence of cerebral injury, even though slight.

If treatment is stopped because of reaction, consultation as to further procedure should be had as promptly as possible, especially for patients with early syphilis.

VII. Special Treatment Problems in Late Syphilis: The treatment of late syphilis must be so highly individualized that no attempt can be made in

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[13] See Appendix VII. The Prevention and Control of Reactions to Antisyphilitic Therapy.

such a publication as this to discuss it in any detail whatsoever. Hepatic syphilis, cardiovascular syphilis, and neurosyphilis, especially, are serious forms of the disease and require expert management. Reference should be had to standard texts [14] for the diagnosis and treatment of late syphilis, and consultation should be sought, if it is available, with respect to the management of any difficult case.

In general, it must be understood that radical "cure" can no longer be accomplished as in early syphilis. The best that can be hoped for is the alleviation of symptoms, the healing of lesions, the restoration and maintenance of health, and the prevention of further progression or relapse. The "arrest" of the process can usually be brought about by systematic treatment of a conservative character.

TABLE 1.—*Schemes for treatment of syphilis discovered in various stages of pregnancy*

Week of gestation	Treatment of syphilis discovered in the first trimester of pregnancy	Treatment of syphilis discovered in the second trimester of pregnancy	Week of gestation	Treatment of syphilis discovered in the first trimester of pregnancy	Treatment of syphilis discovered in the second trimester of pregnancy
1	As [1]		21	As	As
2	As		22	As	As
3	As		23	As	As Bi
4	As		24	As	Bi
5	As		25	As Bi	Bi
6	As		26	Bi	Bi
7	As		27	Bi	Bi
8	As		28	Bi	Bi
9	As		29	Bi	Bi
10	As Bi [2]		30	Bi	Bi
11	Bi		31	Bi	As
12	Bi		32	As	As
13	Bi		33	As	As
14	Bi	As	34	As	As
15	Bi	As	35	As	As
16	Bi	As	36	As	As
17	Bi	As	37	As	As
18	As	As	38	As	As
19	As	As	39	As	As
20	As	As	40	As	As

[1] A trivalent arsenical compound—Arsphenamine in 0.3 gram dose. Neoarsphenamine in 0.45 to 0.6 gram dose. Mapharsen in 0.04 to 0.06 gram dose.

[2] Bismuth subsalicylate suspension in oil in 0.2 gram dose.

VIII. SYPHILIS AND PREGNANCY (*9*): The treatment of syphilis in the pregnant woman is directed entirely toward the fetus, and save for her ability to tolerate treatment, the status of the infection in the mother is to be temporarily disregarded. If the most desirable methods for treating the

[14] See Appendix X. Supplementary Reading List.

mother's infection and protecting the fetus differ (as well they may if, for instance, the mother has general paresis), treatment during pregnancy must be planned for the benefit of the expected child. Proper care of the mother's disease can wait for the few months necessary to secure a full-term, healthy infant.

In the overwhelming majority of cases the pregnant syphilitic woman tolerates antisyphilitic treatment without difficulty. A rare exception to this tolerance is the occurrence of toxic hepatitis and hemorrhagic encephalitis, both of which are very serious reactions. She must be carefully watched for any evidence of intolerance to arsenic as well as for evidence of beginning damage to the liver and kidneys, especially considering the strain already placed upon these organs by the pregnancy. Except as indicated by intolerance, therefore, substandard dosage should not be used, since to do so materially increases the chance of the birth of a syphilitic child.

IX. Congenital Syphilis (*9*): The physician who treats congenital syphilis will do well to select a few antisyphilitic remedies and know them well. Instead of attempting to cover the field of arsenic and bismuth preparations, he will be wiser to choose two or three potent compounds which are low in toxicity and low in reaction-producing capabilities, and administer only these.

Table 2.—*Dose (based on body weight) of 4 arsenicals used in treatment of congenital syphilis*

Drug	Dose	
	Milligrams per kilogram body weight	Grams for 11 pounds (5 kilograms)
Arsphenamine	5 – 7.5	0.025 –0.0375
Mapharsen	0.5– 1.0	.0025– .005
Neoarsphenamine	10 –15	.050 – .075
Sulfarsphenamine	10 –15	.050 – .075

The following treatment system for the treatment of congenital syphilis may be used for children of any age by simply adjusting the dosage on the basis of the patient's weight. It provides for the administration of 34 doses of an arsenical and 43 of bismuth in 72 weeks.

X. Rapid Treatment Schemes: Rapid treatment schemes (so-called "Five-day Treatment," etc.) are still experimental. They should not be used in the treatment of ambulatory clinic patients in any case, and if they are used in hospitals it should be under the most expert supervision. Even then, they should be used only in special emergencies (as in sailors or those who

cannot obtain standard treatment because it is not available), or they should be given as a part of a well-controlled further experimental investigation of the method.

TABLE 3.—*Suggested scheme for treatment of congenital syphilis*

Week	Treatment	Week	Treatment
1.....	Arsenical in one-third to one-half full dose. [1]	29–40...	Bismuth—note overlap.
		41–48...	Arsenical.
2–10....	Arsenical in full dose.	48–59...	Bismuth—note overlap.
10–19...	Bismuth—note overlap.	60–65...	Arsenical.
20–29...	Arsenical.	65–72...	Bismuth—note overlap.

[1] See text, Syphilis in Mother and Child, for a discussion of the desirability of instituting treatment even more cautiously in infants ill with active early congenital syphilis.

CASE-HOLDING AND CASE-FINDING

GENERAL CONSIDERATIONS

Gonorrhea and syphilis are communicable diseases, and every new patient admitted to a treatment service offers to the personnel a double challenge in case-holding and case-finding. These diseases are communicable, however, under very limited conditions, and their communicability may vary or disappear with the passage of time or with treatment. Both diseases may be clinically asymptomatic and still be communicable or potentially so. Communicable relapse of syphilis and reinfection with gonorrhea are common. An otherwise noncommunicable infection with syphilis in a female may become communicable to the infant in pregnancy. Congenital infections are ordinarily communicable only in infancy. Incubation periods are variable and histories of sexual exposure are often indefinite or unreliable. Infectiousness is not easily established by ordinary physical examination; it is likely to be ephemeral, and it is never to be taken lightly since the unexpected may always happen.

Competent medical evaluation of every case is essential to intelligent case-holding and case-finding. It should be obvious, therefore, that those who are to render these services must understand the diseases with which they are to work and must be frequently in consultation with the chief of the treating agency. Reasonably adequate training should be given to all those who are to do this work.

Sympathy, tact, ability to work with patients, and a real interest in venereal disease control are essential in those who are to do case-holding and case-finding. It is important, therefore, that this personnel should be selected with these qualities foremost in mind.[15]

[15] See Appendix I. Qualifications of Personnel.

Case-holding is essential if the patient's infection is to be kept under control until it is cured. It is useless, however, to employ a case-holding staff if the fundamental causes of neglect of treatment are ignored. Some of these are failure to explain the disease, its treatment and its communicability to the patient; failure to take the patient's economic problems and job into account; transportation difficulties; rough or discourteous handling of the patient in the clinic; lack of privacy in the clinic; dirty, crowded, unattractive clinic quarters; poor technics which cause pain, reactions, and resentment; inadequate cooperation between related clinic services, the hospital proper, and the venereal disease clinic so that infections discovered in one service fail to reach the attention of the venereal disease clinic.

An effective case-holding service will be constantly on the watch for neglect on the part of the clinic or other treating agency to *cooperate with the patient.* It should be the ultimate objective of every case-holding service so completely to solve all of those problems which lead to premature interruption of treatment that only those patients who are mentally unable to cooperate or who are obviously antisocial in their behavior need be referred to the health department for control. Except for the truly noncooperative, every patient which the treating agency finds it necessary to report to the health department for control should be looked upon as a clinic failure in case-holding.

If funds are inadequate to provide case-holding services for all forms and stages of infection, first attention should be given to those infections which are actually or potentially communicable. Patients with early or early latent syphilis, pregnant women with syphilis, infants with acute congenital syphilis, and patients who are still in need of active treatment for gonococcal infection, should be the first concern of the case-holding service; for it is these who are the most likely to spread their infections. They must be kept under control.

It must not be forgotten, however, that the adequate treatment of those whose infections are not likely to be communicable is as important to the public health as any other measure which prevents morbidity and death. The prevention of late activity or of disabling end-results, or premature death from venereal disease is as important as the control of cancer, diabetes, heart disease, or any other noncommunicable condition. Thus, although first attention should be given to those whose infections may be spread, the others must be given their share of attention, and a due share of public health funds should be spent for their care. In other words, while it is important to control early, infectious syphilis and to prevent congenital syphilis through adequate treatment of syphilis in pregnant women, it is also the duty of the health department and the treating agency to

assume responsibility for the cure of syphilis or, where cure cannot be attained, to arrest the progress of the disease. It is not fair, either to the patient or to the public health, to give only that amount of treatment which will render the infection even permanently noncommunicable and to dismiss the problem of what may happen to the patient later as of no concern of the health department or treating agency.

On the other hand, it is equally important not to over-treat the patient. There are decided limits of treatment beyond which little or no good may be accomplished, and the patient will be subjected unnecessarily to the risk of serious reaction not to mention unnecessary inconvenience and expense. Altogether too many treating agencies are continuing the treatment of patients for many years simply because blood tests remain positive or because adequate attention is not paid to regular review of case records.

The mechanics of case-holding must vary with the particular problem at hand. Ordinarily, patients with early syphilis who have had enough treatment to render their infections at least temporarily noncommunicable and patients with latent and late syphilis may be followed by letter at first. Postcards should not be used as they are too open for inspection by curious persons, and letters should be mailed in envelopes which do not identify the treating agency as a venereal disease clinic. If there is no response to this form of follow-up, a second or even a third letter may be tried in those latent or late cases which will not likely suffer damage through the additional delay. Those whose infections may become dangerous through relapse, however, should be followed promptly by the field follow-up service. The others may be followed as rapidly as their clinical condition warrants if the field staff is adequate to the load.

Patients with open early syphilis, those who have had so little treatment that any delay may be dangerous, pregnant women with syphilis, and patients with interstitial keratitis or other active lesions which involve vital structures should be followed promptly by the field staff without waiting for results by correspondence. In any case, it should be obvious that whenever there is any doubt as to the urgency of follow-up, the clinic medical director should be consulted.

CASE-FINDING

Case-finding is not an objective in itself. If it is to be of any benefit to the community it must lead to one or more of three conclusions: (1) Better information as to the prevalence or incidence of infection in the community, either for the purpose of stimulating support for an improved control program, or as a measure of the effectiveness of a program; (2) the protection of the public health and the promotion of the public safety, as in the discovery of communicable infection or of cardiovascular or neurosyphilis

in those who hold other lives in their hands; and (3) the treatment of the infected.

Mass blood-testing, in some industries for example, is too often used for the purpose of weeding out infected employees who promptly become candidates for discharge from employment. Food-handlers and domestics, in particular, are singled out for blood tests on the completely false premise that infected food-handlers, because of their occupation, are more dangerous than other persons to the public health. These are abuses of a case-finding procedure which protect nobody and which are almost certain, eventually, to bring this case-finding procedure into disrepute.

It is of the utmost importance, therefore, that the health department do all that it can to see to it that any case-finding procedure is used with an intelligent and legitimate objective in mind.

Case-finding procedures may be divided into three main groups: (1) Mass blood testing; (2) direct epidemiologic investigation, starting with a known infection; and (3) public education, through which those who may have been exposed are encouraged to seek medical advice.

Mass blood testing.—Mass blood testing should be encouraged as a valuable method of case-finding in at least these situations:

1. In hospitals and hospital out-patient departments and in physicians' offices, blood tests should be made of all persons who apply for medical care and whose condition suggests the need for general physical examination. That is, a blood test should be considered as much a routine procedure as the examination of urine, measurement of blood pressure, or taking the patient's temperature. Blood tests should be made of all pregnant women.
2. In industry, where further recognition of syphilis is a valuable method for reducing industrial hazards and insurance loss. Periodic blood testing should be encouraged in industries involving risk of life or injury to the patient or others, or the protection of property. Blood testing of employees in selected industries, however, such as food-handlers, domestic servants, barbers, and beauty parlor operators, serves no special purpose as a measure for the protection of the public against infection. That is, there is no relationship between these occupations and infectiousness, and employees in these occupations should not be singled out for undue discrimination on such grounds.
3. In selected population groups, e. g., the entire population of a county, not only as a method of individual case-finding where the prevalence of infection is high but also as a measure of the extent of the syphilis problem in the community.
4. In enrollees of the Army and Navy.
5. In candidates for marriage.[16]

In all these categories, with the possible exception of (3), the blood test should be part of a general physical examination. The discovery of a positive blood test in any of these categories should not, per se, be the cause for refusal of employment, dismissal from employment, denial of the right

[16] Two members of the advisory committee (Moore and Nelson) feel that for medical, social, and political reasons alike, blood testing compulsorily required by law is at present unwise in any category of patients.

to marry, or disclosure of the existence of the infection to another person. If an actually or potentially infectious person insists upon exposing another, as in marriage against advice, or in other circumstances, the infected person, himself, should be forcibly quarantined.

Direct epidemiologic investigation.—Direct epidemiologic investigation, starting with a known infection, is probably the most productive method of case-finding, at least so far as the discovery of communicable infections is concerned. It is when case-finding is initiated by the discovery of a patient with a recently acquired infection that the greatest promise is offered for communicable disease control.

If every patient could be identified, by name and address, in the original morbidity report to the health department, the problem of how to conduct epidemiologic investigation would be most simple of solution. With the patient as the starting point, the health officer could proceed with case-finding in venereal disease as he does in case of any other communicable disease. Unfortunately, however, it has not proved to be practical to require that the infected be routinely identified to the health department. Physicians very frequently will not report their patients by name and address, patients use aliases or give false addresses, and it has been understandably impossible to convince the public that its infections with venereal disease should become the routine, public business of the official health agency. Infection with syphilis or gonorrhea cannot be separated from the implication of sexual misbehavior, from the patient's point of view. He is too well aware of how his infection will be interpreted by his friends and neighbors, and he looks upon his identification to the health department as the first step toward public identification as a violator of the moral code.

Most States protect the patient's identity so long as he continues treatment. Many, however, require the identification of the patient's contacts to the health department. This, we believe, is unsound. The contacts deserve the same confidential handling as the patient until it is obvious that they will not cooperate. The chief difference between the patient and his contact is that the former, often quite by accident, has had his infection identified and is receiving the benefits of treatment. There is no justification for the subjugation of the contact to the public gaze when the patient is protected from it. A patient's contact (his infected wife) deserves the same confidential consideration which he, himself, has received.

The identification of alleged sources of infection and of some other contacts depends upon the disclosure of sexual indiscretion in the majority of cases. Those who are so identified must be approached and advised to seek medical attention. They may be embarrassed and perhaps even angered or frightened by the patient's failure to respect a confidential personal relationship. Women named as contacts, whether married or single, require much more delicate and tactful management than men.

Most contacts, men and women alike, are ordinarily decent citizens who must be treated, not as sinners, but as persons actually or potentially infected with a dangerous communicable disease.

If the health officer enters the picture, he intensifies the fears of those who are named as contacts, thus increasing their resistance. By virtue of his official status it is implied that the matter has become one of public record. This is a particularly serious matter in small communities, where the patient or the contacts may be well known to the whole health department personnel, and where gossip is not unknown. Moreover, since the health officer lacks the highly personal physician-to-patient relationship enjoyed by the private physician, or even the clinic physician, he is less capable of dealing with the intricate personal and social problems which a diagnosis of syphilis or gonorrhea may involve.

For these reasons, direct epidemiologic investigation is best carried out by representatives of the treating agency, in the name of the treating agency. Only the patient can supply the information by which his contacts may be identified. The clinic follow-up worker has the confidence of the patient and will often be able to obtain the patient's active assistance in bringing the contacts to medical attention. In many cases more than one contact must be investigated, although not all of them will be found to be infected. It is much less disturbing to those who must be approached that the approach is made by a representative of a medical agency: There is then an implication of the confidential relationship which is commonly accepted as characteristic of medical agencies. This softens the blow and makes the investigation a medical, rather than a public, and possibly punitive, one.

MECHANISM OF CASE-HOLDING AND CASE-FINDING

In hospital out-patient departments.—In large urban clinics where the clinic load warrants, full-time follow-up workers should be employed for case-holding and case-finding. They should be responsible to the clinic physician-in-chief directly, or through the chief of the nursing or social service to whom they may be responsible. It is their function, primarily, to control communicable disease and to promote the adequate treatment of the infected, whatever the stage or form of their infections. Problems in social case-work should be referred to the department of social service.

If the load does not warrant the employment of full-time workers, a single worker may serve two or more clinics, or the part-time services of a nurse or medical social worker may be engaged from some other agency.

In any case, the worker should be employed by the agency which administers the clinic; not by the health department and assigned to the clinic. Her salary and expenses should be included in the clinic budget and be charged to the cost of clinic maintenance, toward which the health department may contribute through full or partial subsidy.

If several clinics serve a common area, it may be convenient to divide the area into follow-up districts, in each of which one worker will do all the work for all of the clinics.

In health department clinics.—If the clinic load warrants full-time follow-up service, and the community is so large that the follow-up worker will not be too readily identified by the public with the venereal disease clinic, the follow-up service should be organized and should function as it does in a hospital clinic. If health department nurses are assigned to this duty, their relationship to the clinic should be that of any nurse to any medical agency. They should in no way represent the health department as an enforcement agency. Incorrigible and uncooperative patients should be referred to the health officer for control, just as they would be from a private clinic. That is, the clinic as a treating agency, should be quite separate and distinct from the health department as an enforcement agency.

If the clinic is small, or there is risk that a special venereal disease clinic worker would be identified by the community as such, the health department nurses who do generalized nursing may be assigned to do clinic follow-up work as a part of their general nursing duties. They should be assigned to regular duty in the clinic itself, however, so that they may become familiar with clinic routine, with clinic patients and their problems, and learn to represent the clinic as a treating agency. These nurses should never be used as enforcement officers, for enforcement and treatment functions cannot be carried out by the same person in venereal disease control where maintenance of the patient's confidence in the treating agency is so important.

In mobile units the district or county nurse who represents the unit in its other functions (prenatal, etc.) should also do case-holding and case-finding. If special nurses are engaged for venereal disease follow-up in rural areas they are certain to become identified with this particular service, and their visits to the infected and to their contacts are certain to become unwelcome.

In prenatal clinics.—If a prenatal clinic is unable to provide adequate follow-up service for pregnant women with syphilis through its own personnel, the part-time services of the venereal disease clinic worker may be utilized. If several prenatal clinics in an area are in need of this service, a full-time worker may be employed by all of them, jointly. The health department should reimburse private prenatal clinics for this service if it involves the employment of special personnel, but the clinic should employ the worker and administer the service. If the prenatal clinic is operated by the health department, the follow-up worker should have the same relation to the clinic as the health department follow-up personnel in a health department venereal disease clinic.

In private practice and institutions.—Whether a confidential case-holding and case-finding service can be provided through health departments to private physicians and institutions, on a sound economic basis, has not yet

been determined. It is possible that it may be economically sound in highly urban areas where concentration of cases to be followed is great enough to keep the cost of travel down to a reasonable level.

If it is attempted, trained workers should be employed to do the follow-up work in the name of the physician or institution; not as a representative of the health department. No patient or contact thus followed should be identified to the health department except as the physician, himself, may decide for legitimate cause. The worker should be as subject to the reasonable direction of the physician and should as fully protect his patients as if she were employed and paid by the physician.

It is possible that where private visiting nurse associations exist in the less urbanized areas, or where physicians have been persuaded to use health department nurses for prenatal or other general nursing services, this confidential venereal disease follow-up work may be done by these nurses at the expense of the health department. Patients and contacts who recognize these nurses as associated with private or public agencies should be reassured that this particular service is being rendered for the physician on an entirely confidential basis and not as an agency service. The identities of the patients or contacts followed should not be disclosed by the nurse to either the health department or the visiting nurse agency with which the nurse is affiliated. It is the duty of the physician to report any uncooperative patient to the health department.

However this service may be offered, adequate statistical data should be collected concerning the types of cases followed and the results of follow-up to permit of evaluation of the service.

Information and Education

Professional

Medical.—The control of the venereal diseases will depend, in great measure, upon how well the medical profession is informed and trained in the management of these diseases. Whether the physician is engaged in the private practice of medicine, in the treatment of patients in a venereal disease clinic, in medical teaching, or as a health officer, it is he who will make the diagnosis and treat the patient or conceive and direct the control program. It is a matter of fundamental principle, therefore, that the health department give adequate attention, in the development of its venereal disease program, to the following procedures in medical information and education:

1. The modification of the curriculum of the medical school toward better instruction in the public health aspects of venereal disease control. This will not be accomplished by the mere simple presentation of the facts, however sound or cogent. It will require a judicious, tactful and diplomatic

approach to the many conflicting interests and viewpoints affecting a medical faculty. The establishment and maintenance of a lasting and influential alliance between medical education and public health will hardly result from a single effort, however high its source. The Surgeon General of the U. S. Public Health Service has attempted, and should continue to attempt, to demonstrate that medical education holds a vital position in the venereal disease control and the general public health programs. The Public Health Service and State health departments should continue to study and to encourage improvement in venereal disease control teaching methods in the medical schools of the United States.

It is believed that a minimum curriculum for the teaching of venereal disease control should be recommended and developed, due regard being had for the broader relationships of the subject to medical and surgical practice through a division between required and elective courses. The required course should consider general methods and interpretations, control of infectiousness, standard diagnostic and treatment procedures in early and latent syphilis and gonorrhea, the general management of late syphilis, prevention of cardiovascular and congenital syphilis and neurosyphilis, prevention of the serious complications of gonococcal infection, the use of drugs, and precise instruction in the details of technic with emphasis on indications, reactions, and contraindications. The detailed consideration of system diagnosis, rarer lesions, intricate (consultant) problems, and the relation of the venereal diseases to the specialties may be left to elective courses.

Because of the important position which the private physician holds in the public health program for the control of the venereal diseases, much stress should be laid upon the public health aspects of venereal disease control in teaching the medical student.

State health departments have an unusual opportunity, through their close contact with State medical licensing authorities, to stimulate medical schools to greater effort and efficiency in teaching venereal disease control. Dilatory medical faculties may be induced to raise their teaching standards in this subject by the insertion of appropriate and searching questions on the modern management of venereal disease into State licensing examinations.

2. Subsidies to medical schools, teaching hospitals, and teaching clinics for graduate and undergraduate medical students. Subsidy may be in the form of salaries for better qualified medical and technical personnel, or for the purchase or loan of equipment to be used in teaching and research in this field. Federal funds for venereal disease control, allocated to State health departments, may in turn be allocated by the latter to medical schools, teaching hospitals, and teaching clinics in order to support and improve medical educational facilities in the respective States.

3. Postgraduate instruction of practicing physicians. Although this is secondary to better instruction of the medical student, it is none-the-less of great importance. Two types of activity should be fostered—the short review course in current diagnostic and treatment practice, and the prolonged, intensive training course for the future specialist (and especially clinic medical personnel). For the former, State health authorities are urged to study the possibilities and to take the necessary local measures. The Public Health Service is urged to expand the provisions for the latter. Any tendency to confine instruction to the control of syphilis, alone, should be vigorously combatted if equally important advances are to be made in the control of gonorrhea and the other venereal diseases.

4. The provision of consultation services. Whether these are within or without the personnel of the local, State or national health organizations, their provision should be given special attention. Recognized standing as a consultant should be prerequisite to appointment; adequate remuneration should be provided; a study should be made of the applicability and technic of consultation by correspondence; the possibilities of a traveling consultant staff, with personal conference and examination of patients at appointed times and places should be considered; and the development of such a consultant service on a regional basis, in coordination with treatment centers throughout the State is especially advised.

5. The dissemination of informative literature to private physicians. This is essential. The material used should be so selected that it will aid them in their private practices. It will help to secure their active cooperation in the control program. The monthly journal, Venereal Disease Information, of the United States Public Health Service, continues to prove of value, as do its several medical supplements; their circulation should be increased as far as possible. Appropriate reprints from this journal and from other sources should be distributed to physicians from time to time.

This educational material should be interesting, scientific, and brief. It should deal with some special problem in diagnosis, treatment, or aftercare which the group for which it is intended frequently meets in routine work. From time to time physicians should be sent copies of the material used in public education in order that they may be encouraged to supplement, by personal instruction, the influence of these pamphlets. To every physician who treats the venereal diseases there should be sent a supply (with invitation for renewal) of suitable material for the information of his patients. It is of great value to the physician to have his instruction of the patient supported by the public health agency.

As a corollary to medical information and education, it is important that the health department should take positive steps toward recruiting specially interested and unusually competent physicians into its ranks and into other functions in venereal disease control. It is recommended that special health

officers with suitable personality, experience, and knowledge be delegated to seek out eligibles from among hospital interns. Such officers should hold sectional and local conferences, arrange special instruction, and by other means, e. g., circularization of current informative material, develop the interest and effectiveness of these interns in this field.

Teaching institutions might also be requested, annually, to supply the health department with the names of undergraduate students whose evident interest in the work might be encouraged and extended in similar ways.

It is also of importance that the health department arrange for conferences and scientific meetings for personnel dealing with venereal disease. State health authorities are urged to communicate with the Public Health Service regarding the development of such conferences. Special consultants and speakers of particular effectiveness should be made available for such meetings.

Allied professions.—Provision should be made, also, for the training and information of nurses, social workers, and public health workers both in training schools and by postgraduate instruction along lines analogous to those followed in the information and training of undergraduate and graduate medical students and practicing physicians. It is from this group that clinic nurses, follow-up workers, health education personnel, and others who will function in one way or another in venereal disease control, will be recruited. It is as important that they, as well as physicians, understand the venereal diseases and control procedures.

PUBLIC

Intelligent public understanding of the venereal diseases and of the objectives of the venereal disease control program is essential to public support of the program and to effective public use of the diagnostic and treatment facilities which are available. Effective and persistent public education not only accelerates case-finding and improves case-holding, but it also may be counted upon to inhibit exposure and to encourage prophylaxis against infection.

Virtually all media of public communication—the press, radio, motion pictures, lectures, publications, exhibits—are as available and as effective in venereal disease education as in any other field of public health. Much is being done with these instruments throughout the United States. The United States Public Health Service is prepared to offer assistance to health officers who wish to revise their old educational programs or to establish new ones. For this purpose, the Public Health Service has engaged trained collaborators of wide experience in the educational field. The Service is engaged, furthermore, in an evaluation of educational instruments and technics. A series of publications, posters and exhibits has already been prepared, after careful analysis of the various audiences for which they

are intended and after study of the responses of the audiences it was desired to stimulate. The Service is also engaged in an investigation of the knowledge, attitudes, and opinions of various population groups, including both healthy individuals and persons under treatment for the venereal diseases. This study may provide a measure of the effectiveness of the educational program as carried on at the present time and furnish a basis on which to build the future educational program.

Great care should be taken to give the public the unvarnished facts. Overdramatization should be strictly avoided for the facts are astonishing enough. Overdramatization and exaggeration lead, eventually, to loss of public confidence in the health department when the truth becomes known. They also lead to hasty and ill-advised public response. Too many persons will be denied or removed from employment if too much emphasis is placed upon the communicability of the venereal diseases without adequate definition of when and how they are communicable. It is dangerous to put too much emphasis upon the blood test as an end in itself. It should be made clear that a blood test should form part of every general physical examination, or that a careful examination, including a blood test, should be made if there may have been exposure to an infection.

Ambiguity and statements which may be misinterpreted should be avoided. Statistics should not be complicated, or require interpretations of which the audience to be reached is incapable. They should be adjusted to the conditions in the area to be reached. Statistics which describe conditions which exist in one part of the country may not be at all applicable to conditions in other areas. If data are used which represent average conditions over the country at large, it should be made clear that they are average, and how they correspond with the local situation.

The Charlatan, and the Unethical Pharmacist and Physician

Recent Nation-wide studies by the American Social Hygiene Association in cooperation with the Public Health Service have disclosed that a large number of people are treated, or drugs are prescribed and dispensed for their infections, by unethical drug clerks. Charlatans and unethical physicians, also, treat many patients, especially in the larger cities. Since none of these is trained in the diagnosis or treatment of the venereal diseases, or competent or equipped to evaluate a cure, every effort should be made to protect the infected from this dangerous exploitation.

Although the health officer may win the voluntary cooperation of even the majority of pharmacists through conference with State and local pharmaceutical associations, there will still be a considerable number who will fail to cooperate except as they are forced to by law. In fact, some ethically minded pharmacists who feel compelled by competition to recommend and sell drugs for the treatment of venereal disease would welcome

legislation which would force all pharmacists to give up this business. It should be the aim of the health department, therefore, to promote the passage of laws which will prohibit the sale of these remedies without a physician's prescription.

It will not be enough to prohibit the sale of specified drugs; the sale of any preparation for the treatment of venereal disease without a physician's prescription should be prevented. This would cover the sale of proprietary preparations, of which there are many, as well as of new drugs which may appear from time to time. The Federal Food and Drug Act can prescribe the quality and branding of drugs to be sold in interstate commerce. Many proprietary preparations, however, are manufactured and sold within State limits, and such useful drugs as the sulfonamides may be sold by any druggist so long as they are not misbranded and are of proper quality, unless a State or local law prohibits their sale.

When legislation has been enacted, the health department should make such observations as may be necessary to see that it is observed, and should report any violations to the proper enforcement authority. It may be necessary in some cases to send health department inspectors to certain drug stores to discover whether the law is being obeyed.

The charlatan usually violates medical practice laws already in existence. His control is a matter of law enforcement rather than one of the enactment of new legislation. The function of the health department in the control of the charlatan is to call him to the attention of the proper enforcement agency whenever it can be discovered that he is practicing in the community.

The control of the unethical physician is a problem for the medical profession. What may be considered as unethical practice is often a matter of degree of mismanagement. The old-fashioned "clap doctor" does not bother with the refinements of correct diagnosis. He treats the patient as long as payments are forthcoming or for a specified period for a specified sum, often payable in advance. He is more interested in what he can collect than in the excellence of his management of the disease, although he must enjoy a certain amount of success in symptomatic cure at least, to acquire his large clientele. In the long run, however, except that he bleeds the patient financially, he probably is no more dangerous to the public health than the physician who uses legitimate treatment procedures unintelligently and who is satisfied with symptomatic cure. The problem is largely one of convincing all physicians that if they are to treat venereal disease at all, they should know what they are doing and should treat and evaluate cure according to the best methods available.

The protection of the public against the exploitation of all three, charlatan and unethical or careless physician and drug clerk, may be advanced, also, through public health education. If the public becomes adequately informed as to the proper methods to be used in the diagnosis, treatment,

and determination of cure of the venereal diseases, the infected may be better able to determine at once whether they are in the hands of a physician who knows what he is doing. It should be the constant effort, therefor, of every health department to inform the public as rapidly as possible upon these matters. Every patient seen by an ethical treatment source should be thoroughly instructed in the difference between good and poor management of venereal infections, for informed and well-treated patients make excellent salesmen among their infected friends.

Prophylaxis

It is recognized that local chemical or mechanical prophylactics, scientifically tested and properly applied, are important in the prevention of the venereal diseases. Their use is, in a sense, an emergency measure. Physicians in clinics and in private practice should recognize their positive duty to instruct those who subject themselves to exposure in the value and technic of prophylaxis. Manufacturers of prophylactics should be required to enclose approved directions for their use with every packet.

Particular reference is made to the work of a joint committee (*10*) on the chemical and mechanical prevention of syphilis and gonorrhea, recently appointed by the American Social Hygiene Association and the Public Health Service. The committee reports that chemical and mechanical prophylaxis is one phase of preventive medicine which supplements but does not supplant other activities designed to prevent exposure to infection. The use of chemical and mechanical prophylaxis does not justify any relaxation of efforts to reduce exposure to infection to a minimum by repression of prostitution and discouragement of other forms of sexual promiscuity.

The committee also points out that in case of syphilis and gonorrhea, as well as other communicable diseases, the best and surest way to prevent infection is to avoid exposure. Recognizing that many infections could be prevented, the committee urges that health education should include information, authoritative and dignified, about chemical and mechanical prophylaxis. Health authorities should cooperate with and give encouragement to educational measures instituted by schools, and social, religious, and other community agencies interested in decreasing the number of exposures to venereal disease.

There are many unsolved scientific as well as administrative problems in the field of prophylaxis. As a result, research in this field should be encouraged. Attention should be given by health authorities to the prevention of the sale of worthless products to the public. The provisions of the Federal Food and Drug Act in this regard are most commendable.

The attention of physicians and health officers is called to the report of the special committee on prophylaxis mentioned above as well as to the

discussion of prophylactic procedures in Supplement No. 6 to Venereal Disease Information.[16a]

Prostitution

Venereal disease control is seriously complicated by the difficult problem of prostitution. The control of no other communicable disease is thus obstructed by so complex a sociologic puzzle, responsibility for the solution of which is divided among many agencies of diverse interests, such as health departments, the social hygienist, the sociologist, correctional agencies, the educator, and the police. Where one should begin and the other should cease to function is so difficult to determine that little of a constructive nature has yet been accomplished toward the solution of the major problem.

It would seem on superficial examination that the health department could ignore all the other agencies and proceed with the control of the venereal diseases through epidemiology, provision of treatment, and, where necessary, quarantine. It might be reasoned that "if a prostitute is the source of an infection, treat her; if she refuses to cooperate by refraining from the practice of her profession until she is rendered safely noninfectious, quarantine her."

The solution, however, is not so simple. In the first place, prostitution is a result of complex and deeply rooted biologic urges which will not be easily repressed. It is fostered by complex economic forces which decree that education and the ability to earn an independent existence shall precede marriage; thus legitimate sexual relationships are delayed far beyond the age of sexual competence and desire. It is further fostered by feebleminded-ness or lesser mental incompetence, by environment, by lack of proper recreational facilities, by poverty, and by many other unfortunate conditions of civilization. These perpetual stimulants to prostitution are not subject to epidemiologic control, and as long as they continue to produce prostitutes, there will be a medium for the spread of venereal disease.

Prostitutes may be divided into three broad classifications; (1) the occasional prostitute, who augments a precarious legitimate living by accepting opportunities to earn an extra dollar, a meal, or entertainment by offering herself for intercourse. In this group must also be included the sexually precocious girl, whether feebleminded or not, who indulges in promiscuous intercourse when the opportunity presents itself but who cannot be considered an aggressive, habitual prostitute; (2) the habitual prostitute who is on her own. She frequents beer parlors, road houses, honky tonks, and other places of questionable entertainment or walks the streets in search of susceptible males; and (3) the inmate of an established house of prostitution, or the "call girl" in a system of prostitution.

The occasional prostitute may be susceptible to epidemiologic control

[16a] See Appendix VIII. The Prophylaxis of Syphilis and Gonorrhea.

procedures. She is likely to have a reasonably permanent address, or she often makes her contact with the male she infects at her place of occupation (if she is a waitress), and can be located in one place or the other. Unless she is feebleminded or incorrigible, she is apt to accept treatment and remain under control with some degree of appreciation of her predicament. She may be amenable to rehabilitation if her income can be augmented by legitimate employment. The combination of epidemiology, treatment-control, and rehabilitation should be adequate to the solution of a large part of the problem which this group of prostitutes presents. The feebleminded, the incorrigible, and the sexually precocious girls, however, will be difficult to control and will probably become habitual prostitutes unless they can be permanently confined, or will respond to protracted efforts at rehabilitation.

The habitual prostitute who is on her own usually has no other occupation except as she may have to augment poor professional income by legitimate work. She makes her contacts in places where she may be known to prospective customers as "Alice" or "Cupie" or "Snooks," when her real name is Susie Smith. The resorts which tolerate her are purposely "helpless" to identify her when the epidemiologist (or a policeman) attempts to locate her. She usually compels her consort to rent a room in a convenient and cooperative hotel, rooming house, or regular house of assignation. If she uses her own room (which is rare) she is likely to move from place to place as rapidly as may be necessary to keep at least one broad jump ahead of apprehension, either by the health officer or the police. In some States she is known to rotate from community to community according to a loosely organized plan arranged among a group of her kind. By the time the infection in the consort is detected and epidemiologic investigation begun, she is somewhere else. Not infrequently, she uses taxicabs for her purposes, the accommodating cab driver remaining in the cab or not, depending upon the condition and esthetic requirements of the male customer.

There are even "specialists" among these women who limit the practice of their profession to certain groups of men, particularly sailors. Called "sea gulls," they concentrate wherever ships are in port and travel from port to port as ships move about with their complements of men. Naval authorities declare that they are extremely difficult to identify, being known by nicknames, or to locate, since they travel about so rapidly.

It is difficult to see how epidemiologic procedures, alone, can control the spread of infection by these women. The epidemiologist cannot find them because infected patients can neither adequately identify nor provide addresses for them. They are unlikely to remain under treatment if they are found. If they have early syphilis, quarantine (for at least a year, under regular treatment) will control the further spread of infection with that disease, but gonorrhea can be acquired, and spread, almost immediately upon release and resumption of promiscuous sexual activity. In any case,

the number which can be apprehended for quarantine is now very small. If it becomes generally known that this procedure will be regularly applied, greater precautions will be taken to avoid apprehension. Many of these women prefer to be prostitutes and are not amenable to rehabilitation.

An efficient policeman in plain clothes should, however, be able to find any promiscuous woman that an ordinary man can pick up, even though it is conceivable that a specifically designated prostitute might escape apprehension for some time. Little will be accomplished so long as the health officer remains the only stimulus to police activity through reporting to the police the "names" and descriptions of these migrating prostitutes. When the police are compelled by public demand to take effective action, they will attack the problem from the direction of ridding the community of all prostitutes, migrant or resident, instead of from the direction of apprehending, for the health officer, only those who have been described as probable sources of infection with venereal disease. It is a function of the health officer to persuade the public that this is a police problem and not one of epidemiology to any practical extent.

The ultimate solution of the problem which these women present is, of course, for the sociologist to find. It must be determined what causes them to become prostitutes and preventive measures applied before they acquire the habit.

This does not relieve the health officer of the responsibility of controlling all he can trace through epidemiologic processes, but it is most unreasonable to drop the problem of repression into his lap as a public health matter, and to express surprise or indignation upon the discovery that he has been unable to do much about it.

Organized prostitution is a part of a great, underworld racket. It is mixed up with politics, graft, and police protection and too often tolerated by a public which looks upon it as a necessary protection for the "good" girls in the community who would otherwise be the frequent victims of rape. It is constantly recruiting new girls to the profession and transferring the regulars from house to house to avoid their apprehension. It engages the services of pimps (including hotel porters, bell hops, elevator men, taxicab drivers, and others). If open houses of prostitution are not tolerated, it employs "call" girls, who live in their own apartments and go to their customers on receipt of a call from a "central office," which may be the private home of the madame.

No epidemiologic procedure in the hands of the health officer can solve this problem. Even though it were possible to trace an infection to a particular girl in a specified house, the incubation period (of syphilis at least) is so long that many infections will have been caused by a busy girl before the health officer can even start the epidemiologic process. If a whole house of prostitution is quarantined (as has been spectacularly done in at

least one large city), the health officer may be forced to prove that it is a house of prostitution. It is the function of the police, not the health officer, to raid. If the health department is forced to take over the function of the police, it may well degenerate, eventually, into the same "protective" agency that the police in some places are alleged to have become. In fact, where the health department "supervises" prostitution by the examination of prostitutes the degeneration is already evident. [17]

No health department should ever engage in the medical supervision of prostitutes. Aside from the fact that the health department should not thus become a partner in an illegal and immoral enterprise, the medical supervision of prostitution has been completely exposed as utterly useless. Infection is too difficult to detect by any system of routine examination; exposure between examinations is too frequent to make the procedure effective; and it is likely that graft, inefficiency, and favoritism will quickly nullify even the slightest value the measure might have as they always do wherever an attempt is made to regulate vice.

Neither should health departments combine with the police or the courts to determine whether a prostitute should be sent to jail or released, depending upon whether or not she is infected. The nature of the punishment for prostitution should be determined without consideration of the element of infection. When the punishment has been determined, the disposition of the medical problem may be decided. If the prostitute is jailed, the correctional institution to which she is sent must arrange for her treatment

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[17] The Conference of State and Territorial Health Officers has issued the following statement with reference to the relationship of the police and the health department to prostitution as a source of venereal disease (May 9, 1940):

"There is agreement that failure to control sources of infection in any campaign against syphilis and gonorrhea favors the spread of these diseases. It is known that many persons who are infected with syphilis or gonorrhea * * * acquire their infections from prostitutes or from persons who have been infected by those practicing prostitution.

"It is also generally accepted that the licensing or toleration of prostitution and of agencies promoting prostitution increases the opportunities and accessibility of prostitutes and the volume of their promiscuity. Furthermore * * * nearly all States and cities have laws or ordinances declaring commercialized prostitution to be an offense against public order and morals * * *.

"These governing facts should be applied to questions arising out of the concentration of military and naval personnel for purposes of training and national defense in many States; and to similar questions arising from [permanent] temporary, or transient concentrations of industrial and other population groups * * * health authorities should endorse these views and the conclusion that success in the control and reduction of prostitution is clearly an advantage to the public health.

"* * * it should be made clear to the public that police and court authorities are responsible for the repression of prostitution, whether commercialized or clandestine in character, but that local, State, and Federal health officers may be counted upon to cooperate with police and court authorities and voluntary agencies in achieving practical results in such repression."

(although it may be at a health department clinic). If she is placed on parole or probation, the parole or probation officer must supervise her treatment so long as she is in his charge. If she is freed, she returns to the community with all of the rights of any citizen, and the health department becomes responsible for her control as it is in the case of any other infected citizen and upon exactly the same basis.

All this simply faces the fact of prostitution. It does not solve the problem of what to do about the prostitute as an "antisocial" person. She deserves the greatest sympathy for the predicament she is in, whether she is capable of appreciating sympathy or not. She is too often the victim of mental inadequacy, environment, sex precociousness, poverty, lust and greed, and many other conditions. A society which continues to fail to remove the causes of prostitution, or to protect those who are incapable of protecting themselves, is as "antisocial" as the prostitute. She is the product of society's own neglect. It should be the policy of every health department to encourage those agencies which are looking for the solution of the fundamental social problems which produce the prostitute. If more attention were paid to the correction of these conditions, there would be hope that the present brutal hounding of the prostitute by the police and society alike might no longer be necessary.

Although prostitution, so long as it exists, will remain a vehicle for the spread of venereal disease, and an ultimate source of infection in the community, the health officer will do well to remember that syphilis and gonorrhea are spread widely in the population by average members of it who cannot be considered prostitutes in any sense. Husbands, infected through occasional sexual indiscretions with female friends or acquaintances, in turn infect their wives. In like manner, some wives bring infection home to their husbands. Boy and girl friends spread infection to each other. The epidemiology of these infections is, or should be, much simpler than the epidemiology of infection acquired from most prostitutes, for these occasional and "friendly" contacts are much more readily identified and located.

Better public education leading to prompt medical attention for any infection, whether acquired from a prostitute or a friend, and thorough epidemiologic investigation of at least every recent infection will, if combined with adequate treatment, effectively control the spread of venereal disease. If prostitution could be completely wiped out, or even thoroughly repressed, the control problem would be much simpler, but it should be by no means impossible to prevent the greater part of the spread in the general population by educational and epidemiologic procedures.

It behooves the health officer, therefore, while he continues to insist upon the repression of prostitution, to apply with all the vigor at his command those public health procedures which it is well known will produce excellent results.

THE PROBLEM

Experience has taught us that gonorrhea and syphilis are dangerous saboteurs of national defense. They waste man-power and destroy the effectiveness of Army, Navy, Marine, and Air Corps personnel and of civilians engaged in essential defense industries. More than 7,000,000 man-days were lost to our armed forces during World War I as a result of infection with venereal disease, and a great epidemic of these diseases swept over the entire world during and shortly after the war.

Although great strides have been taken since then toward the development of a peace-time control program and although there is considerable evidence that the prevalence of venereal disease has been greatly reduced, it is certain that the present congregating of large bodies of men for national defense will result in a serious reacceleration of the spread of infection.

It is fortunate that the country is now much better prepared to cope with the problem than it was during the last war. The diagnosis and treatment of both gonorrhea and syphilis have been greatly improved. There are thousands of public clinics today where there were only a few hundred then. Every State has a control program, and the public has accepted venereal disease control as a legitimate function of health departments everywhere. It will not be necessary, as it was last time, to set up overnight an emergency program built solely upon the premise that military men must be "kept fit to fight."

At the same time, those who exploit the prostitute have also improved their technics. It has been said that as the Army has become mechanized, the prostitute has become motorized. It served reasonably well during the last war to police relatively small areas in the vicinity of military establishments, but the automobile has extended those areas almost without limit. Road houses, taverns, dance halls, and other purveyors of entertainment within automobile range of camps or defense industries will serve as centers from which the prostitute may operate. Large cities, where vice may be more easily organized and covered than in small towns or in rural areas, will be within easy reach of many camps. Civilian employees in defense industries, for whom no provision is made for recreation after working hours, will be free to spend their money for whatever entertainment the community in which they find themselves may have to offer.

Many forces are being gathered together and organized to meet these new conditions. The Army is providing entertainment at the camps on a scale never before attempted. The Federal Security Agency has gathered

various national service agencies into a group [18] which is raising voluntary funds for the maintenance of welfare and recreational facilities in civilian areas for the use of military men on leave, and it has set up a service [19] which aims not only to combat the influences of vice but to do something for the rehabilitation or control of girls and women who have or may become involved in prostitution. Everywhere, throughout the country, State and local defense committees have been set up which have as their objective the solution of those problems which arise out of the new conditions created by the national defense program.

Congress has recognized the importance of controlling prostitution in areas within reach of military establishments by enacting legislation [20] which authorizes the fixing of limits within which prostitution may be prohibited and offenders tried in the Federal Courts.

The Army has relaxed or abolished several of its regulations which provided for punishment for acquiring venereal disease and which tended to encourage concealment of infection. The infected are still subject to loss of pay during hospitalization, however, and are likely to be confined in the hospital for unnecessarily long periods, which still tends to encourage concealment. The Subcommittee on Venereal Diseases of the National Research Council is in regular conference with representatives of the Army, Navy, and Public Health Service in an effort to iron out "kinks" which still exist.

One problem to which this group (and the Conference of State and Territorial Health Officers) has given special attention is that of the status of candidates for selective service who have gonorrhea or syphilis. It is probable that, since the sulfonamides effect the cure of gonorrhea in so high a proportion of cases within a very short time, men with gonorrhea will be accepted for induction and will be treated by the Army.[20a] Those with early or latent syphilis will probably be accepted when they have had that amount of treatment which the Army insists that infected soldiers shall have. The further question as to what shall constitute adequate treatment of men infected during their period of service, before they may be returned to civil status, is being given careful consideration.

There are many problems for the various public health agencies to solve, and there are others for the solution of which the combined efforts of the

[18] The United Service Organizations in which six national agencies—the Y. M. C. A., Y. W. C. A., National Catholic Community Services, Salvation Army, Jewish Welfare Board, and Travelers' Aid—have membership. Its purpose is to provide services in civilian areas which will help to maintain the morale of soldiers and sailors on leave without the confusion and duplication which would occur if each agency carried out a program of its own.

[19] The Division of Social Protection.

[20] See APPENDIX IX. The May Act.

[20a] The Surgeon General of the Army has accepted the principle that men with acute gonorrheal infections will be accepted but only when the War Department has made provision for their treatment after they are inducted.

public health agencies and various welfare and service organizations will be needed. Since defense is a national problem, every health agency, from national to local, will have to share the responsibility for carrying out the venereal disease control program.

THE UNITED STATES PUBLIC HEALTH SERVICE

The national defense program involves the collection of men from all parts of the country and their concentration within relatively small areas, whether in military establishments or in defense industries. Immediately upon their arrival in those areas there is created a great public health problem, not only within the camp or industry but also in the surrounding civilian communities. Most of the communities immediately adjacent to these camps and industries are small and unable to cope with the emergency, either then or later. Many of the States in which these men are concentrated are economically unequipped to undertake adequate health programs even in times of peace. It is unreasonable to expect that these communities and States shall assume the entire burden of providing the health services which will be so suddenly and so overwhelmingly in demand.

It has already been said that defense is a national problem. The Congress should recognize that the Public Health Service has as important a function in the national defense as the Army or Navy or any other arm of the military service. Whenever men are to be concentrated, whether in camps or in industry, the Public Health Service should move in to provide and supervise those services which will be needed, over and above the normal requirements of the civilian population in peace time. Emergency appropriations should be made for this purpose exactly as they are made for the expansion of the military services.

The Service should not take over, or unreasonably interfere with, the functions of the local authorities. It should superimpose its own services, under its own direction, wherever local facilities are inadequate and augment local services when they are good and need only to be expanded. Its program should include not only the provision and protection of food, water supply, sanitation, and general communicable disease control but, also, a complete program of venereal disease control where such a program does not exist, is basically inadequate, or needs simply to be expanded.

STATE AND LOCAL HEALTH DEPARTMENTS

So far as direct (epidemiologic and therapeutic) control procedures are concerned, a plan has already been agreed upon [21], through the Conference of State and Territorial Health Officers, which depends upon full cooperation between State and local health departments, the War and Navy

[21] See APPENDIX X. An agreement by the War and Navy Departments, the Federal Security Agency, and State Health Departments.

Departments, and the Federal Security Agency. Upon this plan, which should be considered as constituting a minimal program, a more nearly complete program should be built.

First, attention should be given by State and local health departments to diagnostic and treatment facilities in the civilian areas which will be affected by the presence of military establishments or defense industries. Where there is an increase of any consequence in civilian population, existing diagnostic and treatment facilities may be inadequate. New clinics may have to be established or existing clinic services expanded. Adequate case-finding and case-holding services should be provided in parallel with the expansion of treatment services. If prostitution becomes a problem and the police are sufficiently active in their attempts at its repression, the health department may find it necessary to cooperate with prison authorities or other correctional agencies in the provision of adequate treatment for infected prisoners, probationers, or parolees. While it should be the function of the correctional agency to provide this as well as other medical services to its wards, it is quite likely that this highly specialized service may not be available except as it may be provided through the health department.

Second, the health department should acquaint the public, and especially that part of the population which has newly arrived, of the existence of these diagnostic and treatment facilities and their purpose. This is especially important in defense industry, where little if any provision is ordinarily made for the management of venereal disease.

Finally, so far as the civilian population is concerned, the health department should carry on a campaign of public information which will be calculated to arouse public opinion against prostitution and for its rigid repression by the police, and which will stimulate prompt and effective provision by the community of recreational facilities, not only for soldiers and sailors on leave, but for nonresident employees of defense industries in particular. The stranger in any community who, in his spare moments can find no wholesome entertainment, will hardly walk the streets very long with his hands in his pockets. He soon becomes the ready victim of those who exploit the more vicious forms of entertainment for profit. The health officer who would prevent much of the infection, which is certain, otherwise, to occur, will do everything within his power to stimulate the community to the provision of wholesome recreation and entertainment, constantly available, for these men. This is as important to the maintenance of a high moral standard as it is to the maintenance of good morale.

The Army and the Navy will provide adequate treatment facilities for infected personnel. Prophylactic outfits will be generally available and prophylatic stations will be set up in many places. (Civilian general hospitals, at least, and other medical agencies which are open at night should

be prepared to administer prophylaxis on request.) The actual prophylaxis and treatment of venereal disease in soldiers and sailors will not need to concern the health department; but there are other directions in which the health department may cooperate effectively with the military authorities.

Few medical officers are trained in the epidemiology of venereal disease. They are not able, furthermore, to follow contacts into civilian areas or to arrange for their treatment and control. It has not been found satisfactory to depend entirely upon the information which infected men will give their medical officers. Too often the soldier or sailor insists that he was "drunk" and that the girl was a "pick-up." It has been discovered through experience in several States that, for some reason or other, infected men are far more likely to give information to civil epidemiologists, especially to trained public health nurses. Since these epidemiologists will have the responsibility for tracing the contacts in the civil community, there is a great advantage in their obtaining the information directly from the infected men.

In many areas it has been found possible to assign public health nurses to camps, forts, marine and naval hospitals, and naval establishments, who are permitted to interview in private all infected men. If these nurses are selected for their training and experience in the epidemiology of venereal disease and for their tact, good sense, and personality, they not only accomplish more than can be accomplished by any other method, but they soon win the complete confidence of the medical officers as well as of the men.

The contacts who are identified may be roughly divided into three groups: (1) Those who live in other States, (2) those who live within the State but are obviously commercial prostitutes, and (3) those who live within the State but are not obviously prostitutes.

Those who live in other States, whether prostitutes or not, should be referred to the proper State or large city health department for investigation, with the request that the result of the investigation be reported back to the referring State health department. Those who live within the State and who are obviously commercial prostitutes should be referred to the proper police authorities for investigation, except that if the follow-up worker can locate certain of them and provide for their treatment and control through the period of infectiousness, she should do so.

The prostitute whom the follow-up worker shall follow should be selected, however. If it appears that she has early syphilis, it is important that she be brought promptly under therapeutic control, and quarantined if necessary. If she is an inmate of an organized house of prostitution and can be exactly identified she should be followed; but the existence of the house should be called to the attention of the police whether or not she can be identified. If she operates from a tavern or similar "base," and cannot be exactly identified, her description and the location of the base of her opera-

tions should be called to the attention of the police. If she has gonorrhea she should be reported to the police regardless of how she operates, for although she may be temporarily removed as a source of infection by treatment and quarantine, she will become a new source of infection soon after her release.

Those contacts who are not obviously prostitutes should always be followed by the follow-up worker until it is clear that they should be reclassified as prostitutes, whereupon they should be handled as outlined in the preceding paragraphs.

There is another direction in which the State and local health department can be of assistance to the military authorities. A number of soldiers, particularly, seeking to conceal their infections from Army medical officers, obtain treatment for their infections from drug clerks or from private physicians. Both pharmacists and physicians should be urged to look upon this practice as, in effect, conniving with the soldier in the concealment of his infection. The pharmacist should neither prescribe for, nor sell unprescribed medication for the treatment of, an infection in either soldier or civilian; and the private physician should cooperate with the Army medical officers, whose responsibility it is to look after the health of Army personnel, by referring soldiers or sailors to their medical officers.

Candidates for selective service who have been rejected because of infection with venereal disease should be followed by the health department just as any other infected civilian is followed. Special attention should be paid to their prompt and adequate treatment, and as soon as it is adequate the Selective Service Boards should be informed in order that the candidates may be reclassified.

Social Hygiene

The social hygiene program is, and should be, concerned with all of those human relationships which are affected by the fact that the human race is composed of males and females. It attempts to encourage those relationships which are good and to discourage those which are bad. Its ultimate objective is to preserve the family. It aims to prepare youth for family responsibility and to remove those influences which tend to disrupt the family.

Although poor social hygiene often leads to infection with venereal disease, it also leads to many other social ills which are by no means the official concern of the health department, and no health department should assume the direct responsibility for a broad social hygiene program. Divisions of social hygiene in health departments are misnamed for the name implies that the health department is concerned with the whole social hygiene program. They should be divisions of venereal disease control.

The health department should consider, however, what part it should play in encouraging the development of the social hygiene program. Gonorrhea and syphilis are symptoms of poor sexual behavior and, thus, of sexual maladjustments. Preventive medicine is fundamentally more sound than curative medicine; if preventive measures are available and applicable, they should never be neglected. It may well be that the gains which the health department may make in the control of venereal disease through direct medical procedures, may be held only if there is some concurrent improvement in sexual behavior.

On the other hand, if through some medical procedure the venereal diseases could be caused to disappear tomorrow, there would still remain all of the fundamental problems of social hygiene. The prostitute would still be a prostitute, the unmarried mother would still remain to be saved from abandonment to prostitution, families would still be disrupted by sexual maladjustments, and youth would still be in need of sex character building. These, and many other problems are the concern of many agencies whose forces, so far as male and female relationships are involved, find common direction in the social hygiene program.

Somewhere between epidemiology and medicine on the one hand and the social hygiene program on the other, there must be a middle ground upon which the health department and the social hygiene society may often meet. The one finds in the prevalence of venereal disease one excellent argument for better male and female relationships. The other may discover that better social hygiene will help to keep the venereal diseases under control. The health department may encourage public support of the social hygiene movement by emphasizing the relationship between its great public health problem of venereal disease and human sexual behavior. The social hygiene society may be of great assistance to the health department in encouraging public support of the venereal disease control program.

Financing the Program [22]

The proportion of State and local health department funds to be allotted to the venereal disease control activities should be sufficient to provide adequate protection for the public against infection. If the venereal diseases are to be controlled, it will be necessary to develop and maintain a control program which provides for the organization and the services described in these recommendations, however modified they may have to be to meet local conditions. Wherever funds are limited, every effort should be made to establish such basic services as diagnostic laboratory facilities, public treatment centers, case-holding and case-finding, and public and professional

[22] The basis upon which Federal funds are allotted to the States, and the minimal program which the State must maintain in order to obtain Federal funds, are prescribed, annually, by the Public Health Service.

education on at least a minimal scale. As more funds become available these services may be built up toward adequacy and others added. Equal emphasis should be put upon the control of both gonorrhea and syphilis. If only a minimal program can be provided, the public should be informed of its inadequacy and every effort should be made to secure the funds necessary for a more adequate program.

In the reallotment of funds by the State health department to local communities, consideration should be given to (a) the population of the community, (b) the extent of the venereal disease problem, and (c) the financial need. If necessary, reported local morbidity rates should be audited through periodic surveys conducted by disinterested agencies, such as the Public Health Service, to determine the true prevalence of venereal disease and to bring special problems to light. Each health department within a State should be given an opportunity to demonstrate its particular needs.

CHANCROID, GRANULOMA INGUINALE AND LYMPHOGRANULOMA VENEREUM [23]

A majority of the States require that chancroid be reported, and a few States provide for the reporting of granuloma inguinale, and lymphogranuloma venereum. Except for these reporting requirements and for the treatment in some clinics of those infections which are recognized on routine examination, little or nothing has been done in the way of developing an organized control program for these diseases.

Although all three of these diseases are more common in warm than in cold climates and are particularly prevalent in the tropics, there is evidence that they may be found almost generally throughout the United States. Negroes apparently have a very much higher rate of infection than whites.

Despite the fact that little is known of the epidemiology of these diseases and although their treatment has been more or less unsatisfactory in the past, they are sufficiently prevalent in many areas so that measures should be developed for their control. The sulfonamides are apparently quite effective in the treatment of chancroid and, to some extent at least, in the treatment of lymphogranuloma venereum. Serious epidemiologic study should be made of the three diseases, services for their treatment should be available in all venereal disease clinics, and every effort should be made to detect infection, at least in those areas where they are likely to be prevalent. It is of the utmost importance to distinguish between them and syphilis, and to prevent, through prompt diagnosis and full use of the available

[23] This section on chancroid, granuloma inguinale, and lymphogranuloma venereum has been adapted from recommendations of the Subcommittee on Venereal Diseases of the National Research Council, and from suggestions by Robert B. Greenblatt, M. D., Professor of Experimental Medicine, University of Georgia School of Medicine.

therapeutic armamentarium, the serious complications which may otherwise occur.

So far as our present knowledge of these diseases goes, it appears that the great majority of infections are acquired through sexual intercourse. Most of the clinical lesions will be found on, or in the general vicinity of, the genitalia. Much of the effective treatment will involve the use of drugs which are now routinely used in the treatment of gonorrhea. Thus, the clinic facilities for the treatment and epidemiologic study of these diseases are already available and it remains only to attempt the diagnosis and to put available facilities to work.

Chancroid

Chancroid is a disease, usually of the genitalia, caused by the streptobacillus of Ducrey. It is characterized by single or multiple lesions (ulcers) with irregular, crater-like margins, somewhat indurated inflammatory base, and a tendency toward the formation of complicating suppurating inguinal adenitis. The incubation period is usually 3 to 14 days.

DIAGNOSIS

It is important to rule out mixed syphilitic and chancroidal infection. For this reason all local medication should be withheld until 3 negative dark-field examinations on successive days have been made of serum from accessible lesions. During this period saline dressings only should be used. A blood test for syphilis should be made, as well as Frei tests and Ito-Reenstierna tests for lymphogranuloma venereum and chancroid, respectively. Blood tests for syphilis should be made at monthly intervals for 6 months following healing of the chancroidal lesions, and dark-field examinations should be made at once in case of apparent relapse, since the incubation period of chancre may be several times that of chancroid.

Laboratory tests for the absolute diagnosis of chancroid itself may be of more value than many observers have been willing to concede. It is generally agreed that the examination of smears from chancroid ulcers for the Ducrey bacillus is of little value, but a number of experienced workers have had good results with smears of pus aspirated from unruptured buboes. They believe, also, that cultural isolation of the Ducrey bacillus can be accomplished if more care is taken and there is greater perseverance than has been the rule. These observers are of the further opinion that the Ito-Reenstierna test is as specific and as informative an aid to the diagnosis of chancroid as the Frei test is in the diagnosis of lymphogranuloma venereum.

TREATMENT

Local.—Accessible lesions should be cleansed with soap and water and dried. They should then be completely covered with powdered sulfanilamide and a loose, dry dressing applied. This should be repeated at daily

intervals until the lesion heals. In patients with tight phimosis and underlying ulcerative lesions, the phimotic preputial cavity should be irrigated twice daily with 1: 5000 potassium permanganate solution.

Systemic.—Administer sulfanilamide, grams 3.0, for 5 days in divided doses at 4-hour intervals. For 9 succeeding days administer sulfanilamide, grams 2.0 daily, also in divided doses. At the end of 14 days, discontinue all chemotherapy.

Practically all cases of chancroidal infection will respond to the treatment just described. In fact, if the lesion does not heal, doubt is cast on the correctness of the diagnosis of chancroid and the patient should be restudied from the diagnostic standpoint and, if necessary, treated surgically.

If new and more adaptable chemotherapeutic agents become available for the treatment of chancroidal infection, they should be accorded the proper place in the treatment schedule.

Surgical.—Surgical procedures, designed to relieve phimosis or paraphimosis, should be resorted to only on the basis of sound clinical judgment.

Chancroidal bubo.—Most of these will subside with systemic sulfanilamide therapy. If extensive suppuration is already present or occurs, the bubo may be aspirated repeatedly with satisfactory results. The point of puncture should be dusted with sulfathiazole or sulfanilamide powder. On rare occasions, in which suppuration is very extensive and the gland is badly swollen and hot, wide incision and drainage is, in the opinion of some, preferable to any other form of local treatment.

Granuloma Inguinale

Granuloma inguinale is a chronic disease characterized by the presence of Donovan bodies in the lesions. Inguinal involvement is usually secondary to a primary focus on the external genitalia. The inguinal lesion begins as a "pseudobubo" which soon ruptures and forms a mass of granulomatous tissue. At first, this is a moderately clean tuft of meaty tissue abruptly raised above the surface, and having well-defined, rolled borders. The tissue has a peculiar resilience, is velvety soft to palpation, and may bleed easily on traumatization. The lymph nodes beneath this mass may show involvement by the presence of Donovan bodies. Later, the inguinal mass becomes vivid in hue and is composed of shining, verrucous, vegetating nodules of granulating tissue which bleeds easily and is surrounded by readily excoriated epidermis. The disease spreads by peripheral extension and autoinfection, often involving the entire genital area. It may involve large adjacent areas of the lower abdominal wall and thighs and may persist for months or years. More attention should be paid to the early characteristics of the lesion if diagnoses are to be made more promptly than they usually are.

DIAGNOSIS

The clinical appearance of a chronic granulomatous process involving the groin and genital area, with little involvement of the lymph nodes, is characteristic of the disease. The finding of Donovan bodies by Wright stain in deep tissue scrapings, or biopsy of a peripheral area of diseased tissue (including a section of normal adjacent skin), confirms the diagnosis.

Lymphogranuloma venereum, chancroidal infection and syphilis should be considered in the differential diagnosis, and the appropriate test for each condition should be performed.

TREATMENT

Tartar emetic is administered intravenously in doses of 0.03 to 0.12 gram (beginning with 3 cc. and increasing to 12 cc. of a 1-percent solution, if tolerated) three times a week, the maximum tolerated dose to be given for 15 doses. A rest period of 2 weeks should be followed by another series of injections.

If the patient has difficulty taking tartar emetic or the lesions have not improved satisfactorily under that drug, fuadin should be given in 5 cc. doses 2 or 3 times weekly until the lesions have healed, and weekly for 6 months longer to prevent recurrences. If the lesions are still resistant, the antimony compound should be changed. If no further benefits are noted, surgical excision is advisable if the lesions are localized. If they are extensive and chemoresistant, X-ray therapy in large and frequent dosage is the last resource. If this fails, the patient will go on to a slow cachectic death. Chemotherapy should be carried on during radiation therapy.

Lymphogranuloma Venereum

This disease concept includes the conditions formerly known as lymphogranuloma inguinale, lymphopathia venereum, climatic bubo, esthiomene, and inflammatory rectal stricture. It is caused by a filtrable virus, probably of multiple strains. Its distribution is world-wide but its prevalence is greatest in the tropics. It is a systemic disease of the lymphatic vessels and structures, usually originating in a trivial and transitory lesion of the penis, vulva, vagina or rectum, which frequently escapes the patient's notice.

The invasion of the lymphatic glands usually occurs from 10 to 30 days after infection but occasionally may be delayed for months. Inguinal adenitis is often bilateral and sometimes subsides without suppuration. During this stage, constitutional symptoms may be noted. Lymph nodes may fuse to skin, resulting in multiple areas of softening, followed by the appearance of numerous fistulae. Extensive scarring accompanies healing. The anorectal syndrome is usually found in the female and is characterized by rectal pain, discharge of blood and pus from the anus, a tendency toward extreme chronicity, and the production of rectal stricture.

Differentiate from malignant tumors, Hodgkin's disease, tularemia, tuberculosis, pyogenic infections, chancroidal bubo, and syphilis.

Specific (Frei test).—In an infected case, intracutaneous injection of Frei antigen, 0.1 cc., gives rise to an inflammatory papule of at least 0.5 cm. in diameter, often with peripheral erythema and some times a central vesicle. The papule appears within 48 hours and persists for several days. If mouse brain antigen or Frei antigen of chick embryo origin is used, control tests are imperative. Without controls, the reactions to these antigens are too commonly read as positive, whereas a control would have produced an identical reaction.

In infected persons the Frei test may give positive results for years. In suspected cases, negative tests should be repeated. After the development of bubo, over 90 percent of positive reactions occur.

Mixed venereal infections should be ruled out by the dark-field examination of material from genital lesions for the causative organism of syphilis. Frequent serologic examinations should be made for at least 6 months after the disappearance of the lymphatic symptoms.

TREATMENT

Local.—Patients with acute inguinal adenitis should be hospitalized whenever possible. The fluctuant nodes may be aspirated, but incision and drainage is never indicated. Radical excision is inadvisable because of the risk of elephantiasis of the scrotum or vulva. Patients with acute anorectal syndrome should be treated in the same conservative manner so far as local therapy is concerned. Patients with rectal stricture are problems for hospital management.

Chemotherapy.[24]—The use of the sulfonamides in the treatment of lymphogranuloma venereum has not yet been established, but there are some clinical indications that they may be of considerable value. If used, they should be employed as follows:

I. Sulfanilamide: Sulfanilamide therapy should consist of the administration of 5 grams of the drug daily for the first 4 to 5 days, followed by a reduction to 2 or 3 grams for an additional 7 days. If the inflammatory symptoms (not residual scarring) persist, repeat the chemotherapeutic course after a rest period of from 10 to 14 days, using the same or one of the allied chemotherapeutic agents.

II. Sulfapyridine: Sulfapyridine should be administered in doses of 3 grams for the first day and 2 grams for the following 10 to 12 days. The course should be repeated following a rest period of 10 to 14 days if clinical evidence indicates active extension of the glandular process.

[24] Sulfathiazole and sulfadiazine are now also being used in the treatment of venereal diseases.

The acute anorectal syndrome should be treated in the same manner as the inguinal manifestations. Stricture or other late complications should receive special consideration.

Biologic treatment.—Frei antigen given intravenously in 0.2 to 0.3 cc. doses every second day may be of value.

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Appendix I

QUALIFICATIONS OF PERSONNEL

Qualifications of the Venereal Disease Control Officer Adopted by the Conference of State and Territorial Health Officers

Whereas an effective campaign against the venereal diseases is largely dependent upon its direction by a thoroughly qualified venereal disease control officer: Therefore be it

Resolved, That the basic educational requirements and special qualifications of venereal disease control officers shall be those adopted by the Conference of State and Territorial Health Officers on April 25, 1939, to wit:

1. The earned degree of doctor of medicine from a reputable medical school and eligibility to examination for medical licensure in the State where service is to be rendered.
2. Not less than 1 year of general clinical experience gained preferably in a hospital of acceptable standards.
3. The satisfactory completion of not less than 1 academic year of work in a recognized postgraduate school of public health, or in lieu of this special training, 2 years of full-time public health work.
4. A period of at least 6 months' intensive training in the clinical management of the venereal diseases in a well-organized postgraduate course, or its equivalent (not less than 1 year of work in a recognized school of public health) if instruction in the clinical management of the venereal diseases constitutes a stipulated part of the course of training in the school of public health.

Minimal Qualifications for Clinicians, Clinic Nurses, and Medical Social Workers

Whereas the qualifications and experience of physicians, nurses, and medical social workers who serve in venereal disease clinics are of the greatest importance in their efficient management: Therefore be it

Resolved, That it is the sense of this conference that it is highly desirable for the qualifications of physicians serving in such clinics to be:

1. An earned degree of doctor of medicine from a reputable school and eligibility to examination for medical licensure in the State in which he is to serve. The physician selected, if not already licensed to practice within the State, should be licensed at the meeting of the board of medical examiners next succeeding his appointment.
2. Not less than 1 year of general clinical experience gained preferably in a hospital of acceptable standards.
3. A period of at least 6 months' intensive training in the clinical management of the venereal diseases in a well-organized postgraduate course; and be it further

Resolved, That it is the sense of this conference that it is highly desirable for the qualifications of a nurse serving in such clinics to be:

1. A graduate from an accredited school of nursing meeting the minimum requirements set by State law; preferably such school of nursing should be connected with a general hospital having a daily average of 100 or more bed patients, and

the necessary affiliations to provide a program of study which should include instruction and experience in obstetric, pediatric, orthopedic, and communicable disease nursing, including the control of gonorrhea, syphilis, and tuberculosis.

2. Eligibility for registration in the State in which she is to serve.
3. Not less than 3 months' and preferably 6 months' experience in a venereal disease clinic of acceptable standards; or, in lieu thereof, not less than 1 year of general nursing experience after graduation from nursing school in a hospital of acceptable standards; and be it further

Resolved, That it is the sense of this conference that it is highly desirable for the qualifications of a medical social worker to be:

1. Graduation from an accredited course in medical social work in an approved school of social work, and
2. One year's supervised experience in the practice of medical social work in a recognized social service department in a hospital or clinic which has an active syphilis control department.

Or in lieu thereof—

1. Graduation from a 2-year course in an approved school of social work, and
2. Three years' supervised experience in the practice of medical social work in a recognized social service department in a hospital or clinic, 1 year of the experience to be in a syphilis control program; and be it further

Resolved, That in the selection of the above personnel consideration should be given to personal qualifications, and only those persons who have tactful personalities and a particular interest in the venereal diseases and in public health be selected.

Minimal Qualifications of the Public Health Nursing Consultant

Whereas the public health nursing aspects of a venereal disease control program are most effective when included as an integral part of the family health program of the community public health nurse; and

Whereas until all public health nurses have had an adequate preparation in venereal disease control, the service of a qualified public health nursing consultant is essential: Therefore be it

Resolved, That the public health nursing consultant in venereal disease control should possess the following qualifications:

1. An earned degree of bachelor of science or bachelor of arts from a reputable college or university.
2. A graduate from an accredited school of nursing meeting the minimum requirements set by State law and connected with a general hospital having a daily average of 100 or more bed patients, and the necessary affiliations to provide a program of study which should preferably include instruction and experience in obstetric, pediatric, orthopedic, and communicable disease nursing, including the control of gonorrhea, syphilis, and tuberculosis, and eligible for registration in the State in which she is practicing.
3. Completion of at least 1 year's approved postgraduate study in public health nursing carrying regular academic credit.
4. Experience of at least 2 years in a general public health agency which provides supervision by qualified public health nursing personnel and preferably experience of at least 1 year as a general supervisor.
5. At least 3 months of advanced preparation in applied venereal disease epidemiology at an educational institution which meets approved standards.

Postgraduate Training of Venereal Disease Control Officers, Clinicians, Cooperating Private Physicians, and Other Public Health and Scientific Personnel

Whereas the postgraduate training of health officers, clinicians, cooperating private physicians, nurses, medical social workers, and laboratory personnel is one of the most effective methods of instructing such personnel; and

Whereas complete familiarity of such personnel with the most modern procedures for the public health control and clinical management of the venereal diseases in their respective fields is conducive to the best type of campaign: Therefore be it

Resolved, That State health officers are earnestly requested to nominate a sufficient number of capable young physicians, nurses, medical social workers, and laboratory workers to take one of the numerous postgraduate training courses now available; and be it further

Resolved, That the number of such personnel nominated to postgraduate training courses by the State health officer be sufficient to meet the needs in the respective fields of the rapidly expanding venereal disease control program in a given State.

Appendix II

U. S. PUBLIC HEALTH SERVICE NOMENCLATURE FOR SYPHILIS

To be used in reporting all stages of syphilis on and after July 1, 1941

This list rescinds all diagnostic terms pertaining to syphilis now included in the U. S. Public Health Service Nomenclature of Diseases and Conditions, Revised 1935.

		Class No.
2100	Syphilis, primary	25
2101	Syphilis, secondary	25
	Syphilis, early latent (less than 4 years since infection)—	
2102	Spinal fluid negative	25
2103	Spinal fluid not performed (diagnosis tentative)	25
	Syphilis, late latent (4 or more years since infection)—	
2104	Spinal fluid negative	25
2105	Spinal fluid not performed (diagnosis tentative)	25
2106	Syphilis, tertiary—Otherwise unclassified	25
2107	Mucocutaneous	22
2108	Osseous	03
2109	Ocular (except optic atrophy)	10
2110	Visceral (except cardiovascular)	07
2111	Cardiovascular—Other	04
2112	Aneurysm (saccular)	04
2113	Aortic regurgitation (insufficiency)	04
2114	Aortitis (uncomplicated)	04
2115	Neurosyphilis—Otherwise unclassified	16
2116	Asymptomatic	16
2117	Acute syphilitic meningitis	16
2118	Diffuse meningovascular	16
2119	Optic atrophy	16
2120	Tabes dorsalis	16
2121	Taboparesis	20
2122	Psychosis with syphilitic meningoencephalitis (general paresis)	20
2123	Psychosis with neurosyphilis other than paresis or taboparesis	20
2124	Syphilis, type undetermined—To include cases in which accurate diagnosis has not been made	25
2125	Syphilis, congenital—Include all manifestations	25
3047	Arsenical poisoning	19
3058	Bismuth poisoning	19
3233	Iodine poisoning	19
3266	Mercury poisoning	19
2200	Spinal puncture for diagnosis or progress	49
	Special therapeutic practices—	
2300	Fever therapy—Malaria	26
2301	Artificial	26
2302	Intravenous drip	26

Primary.—To include those cases presenting the primary lesion of syphilis (the chancre), which have not yet developed secondary manifestation. This diagnosis must be confirmed by dark-field examination, serologic test of the blood, or both. If blood serologic test is negative, the diagnosis of primary syphilis is not permissible without the demonstration of T. pallidum by dark field.

Secondary.—To include only those cases of early syphilis which show one or more of the manifestations of systemic dissemination of the spirochete; for example, generalized enlargement of lymph glands, cutaneous eruption, mucous patches, condylomata lata, patchy alopecia, laryngitis, bone pains, febrile reaction, etc. The chancre may or may not be present and if present may be in any stage of evolution. In early secondary cases the manifestations of systemic spirochetal dissemination are increasing, have attained their maximum, or are waning. This diagnosis must be confirmed by dark-field examination, serologic test, or both.

In early secondary syphilis and in addition to the manifestations listed above, ocular or neurologic complications (iritis, neuroretinitis, acute syphilitic meningitis) should be specially recorded as:—"Syphilis, secondary, manifested by . . ."

Latent.—Secondary symptoms have subsided and the active manifestations of late syphilis have not yet supervened. There are no evidences of syphilis other than a positive serologic test of the blood. Cases will be classified as: "Latent (early or late)—spinal fluid negative" or "Latent (early or late)—spinal fluid not performed (diagnosis tentative)." The date of the negative examination of the spinal fluid will be stated in all cases.

Tertiary.—This classification is to be limited to cases that show active lesions of late syphilis. The lesion may be a gumma or it may be a diffuse process and may involve any organ or tissue of the body. The majority of all patients with tertiary syphilis will fall within six categories:

Mucocutaneous.—Late syphilitic gummatous lesions of skin or mucous membrane.

Osseous.—Periostitis, osteomyelitis, arthritis, synovitis.

Ocular.—Iritis, uveitis, keratoiritis, keratitis, choroiditis, but not including optic atrophy.

Visceral.—Hepatic, gastric, etc., but not including cardiovascular.

Cardiovascular.—To include all lesions of the heart and great vessels. Classify as follows:

Aneurysm (saccular).—Do not use for a fusiform dilatation of the aorta. Specify artery involved.

Aortic regurgitation (aortic insufficiency).—Specify whether with or without cardiac decompensation.

Aortitis, uncomplicated.—To be used only for those patients with symptoms and physical or X-ray signs of syphilitic aortic involvement in the absence of aneurysmal sacculation or aortic regurgitation.

Neurosyphilis.—To include all cases with involvement of the central nervous system, classified as follows:

Asymptomatic.—To be used only for those patients with early or late syphilis who have no symptoms or detectable physical signs of central nervous system involvement, and in whom the diagnosis is based on the routine finding of abnormalities in the spinal fluid.

Acute syphilitic meningitis.—Usually occurs within the first two years of the disease, most commonly as a relapse phenomenon (neurorecurrence), manifested by the usual signs of low grade meningeal involvement, with or without cranial nerve palsies.

Diffuse meningovascular.—This is a catch basket category to include all patients with neurosyphilis who do not fit into other diagnostic categories enumerated. Manifestations to be stated in each instance.

Optic atrophy.—Primary or secondary.

Tabes dorsalis.—Manifestations to be stated.

Taboparesis.—To be used only in patients with definite psychiatric signs of paresis complicated by definite clinically demonstrable evidence of damage to the posterior columns of the spinal cord.

Psychosis with syphilitic meningo-encephalitis (general paresis).—To be limited to cases which show psychic changes in addition to neurologic signs and the characteristic changes in the spinal fluid. Cases with paretic type spinal fluid but without psychic changes will be reported as: "Syphilis, diffuse meningovascular, manifested by . . .", or as some other type of neurosyphilis.

Psychosis with neurosyphilis.—To include neurosyphilis with psychosis other than cases of paresis and taboparesis.

If tertiary manifestations occur which do not fit into one of these categories, diagnose as:

"Syphilis, tertiary, otherwise unclassified"—Specify.

Type undetermined.—To include cases in which accurate diagnosis has not been made. Every effort should be made to make a complete examination and proper diagnostic classification in all cases.

Congenital.—To be limited to cases that show definite evidence of the existence or former existence of the characteristic changes of congenital syphilis, such as interstitial keratitis, Hutchinson's teeth, saber shins and other bone changes, saddle nose, eighth nerve deafness, etc. The congenital origin of syphilis is not to be assumed merely because the time and the circumstances of the infection cannot be ascertained and there is no scar of a primary lesion.

The suggested terms for various drug poisonings are intelligible as they stand.

Spinal puncture for diagnosis or progress.—This should be used in all cases (syphilitic or otherwise) routinely hospitalized for purpose of a spinal puncture.

Special therapeutic practices.—This section has been included for it seemed desirable to indicate special therapeutic practices which necessitate hospitalization.

Appendix III

DIAGNOSIS OF GONOCOCCAL INFECTION BY THE MICROSCOPIC EXAMINATION OF FILMS STAINED BY GRAM'S METHOD[1]

Preparation of Slide

To prepare a film,[2] the exudate which has been obtained on a sterile swab is "rolled out" over the surface of two glass slides by rotating the applicator between the thumb and index finger. The "rolling" procedure is superior to rubbing the swab over the glass surface, because by this method the pus cells remain intact and more gonococci retain their intracellular position. The "films" or "spreads" should be so placed nearer one end of the slide that space remains available at the opposite—etched—end for labeling. The success of the examination depends directly upon the care with which the film was made. Thick films are unsatisfactory and can be avoided by collecting only a small amount of exudate and by rolling the swab over the surface but once. A well-made preparation should be not more than one cell thick. When the slide has been air-dried and the film fixed by gentle heating of the reverse side of the slide, it should be marked plainly with the patient's name, the source of the specimen, and the date.

Staining of Films

For the examination of films, the only reagents necessary are those required for the Gram stain. The procedure recommended is Hucker's modification of Gram's stain, inasmuch as this has been found satisfactory, and, furthermore, has the approval of the Society of American Bacteriologists.

The films should be stained individually for the best results, although when large numbers are to be examined, they may be stained in groups by the use of slide holders. It it is necessary to do them collectively, those containing thick films should be removed and stained separately, as they require more decolorization than slides with thin films.

HUCKER'S MODIFICATION OF GRAM'S STAIN[3]

AMMONIUM OXALATE CRYSTAL VIOLET

Solution A

Crystal violet (85 percent dye content)	4 gm.
Ethyl alcohol (95 percent)	20 cc.

Solution B

Ammonium oxalate	0.8 gm.
Water	80 cc.

1. Dilute solution A 1–10 with distilled water.
2. Mix 1 part solution A with 4 parts solution B.

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[1] From Diagnostic Procedures and Reagents. Technics for the laboratory diagnosis and control of the communicable diseases. Standard Methods Committee on Diagnostic Procedures and Reagents. New York, Am. Pub. Health Assoc., 1941, pp. 91–93.

[2] The word "film" has been substituted for the word "smear" in the original text.

[3] Formulas are taken from the Report of the Referee on Gonorrhea and the Gonococcus for the Standard Methods Committee on Diagnostic Procedures and Reagents of the American Public Health Association. Year Book 1936–37, Supp. to Am. J. Pub. Health: 27: 126–128, March 1937.

Lugol's Iodine Solution

Iodine	1 gm.
Potassium iodide	2 gm.
Water	300 cc.

This solution deteriorates on standing in the laboratory and should be prepared fresh at least every 2 weeks.

Counterstain

Safranin (2.5 percent solution in 95 percent alcohol)	10 cc.
Water	100 cc.

1. Stain 1 minute with crystal violet solution.
2. Wash in water.
3. Apply iodine solution for 1 minute.
4. Wash in water.
5. Decolorize in 95 percent alcohol for 30 seconds with gentle agitation, or until violet dye fails to appear in the alcohol.
6. Wash in water.
7. Apply counterstain for 10 seconds.
8. Wash in water, blot dry, and examine with oil immersion objective.

To control the staining reaction of each preparation, one loopful of a young broth culture of *Staphylococcus aureus* and one of *Escherichia coli* are placed on the slide before staining. Organisms from solid media may be used if properly diluted with distilled water. While it may not be necessary to control each Gram stain in this manner in laboratories where numerous examinations are made daily, this provision is essential for laboratories in which only an occasional film is examined.

Microscopic Examination

A good compound microscope equipped with a mechanical stage and an oil immersion ens is essential for making a satisfactory examination. When correctly stained, the lnuclei of the pus cells should retain some of the violet dye, while the cytoplasm should be pink. The cxaminer notes first the staining reaction of the staphylococci and colon bacilli placed on the slide for control. (Staphylococci are Gram-positive, i. e., retain the ¡nitial violet dye; colon bacilli are Gram-negative, i. e., do not retain the initial dye, but are decolorized and appear pink from the effects of the counterstain.) If the control films are not properly stained, the preparation is unsatisfactory for diagnosis.

The gonococcus is typically Gram-negative when correctly stained and appears as a pink or orange-red coccus, usually arranged in pairs. The approximating surfaces are flattened, producing the well-known biscuit or coffeebean shape. The organisms may be observed inside or outside of the pus cells. The intracellular location is typical and has considerable diagnostic significance. Extracellular gonococci, as a rule, are found only in films from chronic cases of the disease.

The entire film should be examined for gonococci. For an experienced observer the period of examination should be at least 3 minutes, preferably 5. Special care is required with vaginal and cervical films from chronic cases in order to avoid missing the occasiona gonococcus. All slides should be filed and kept for at least 6 months. While making the examination, the absence or presence of pus cells and their frequency should be noted. If spermatozoa are observed, this fact may also be recorded.

Reporting Results of Examination

The responsibility for interpreting the results of a microscopic examination is solely that of the physician in charge of the case. The laboratory examiner should report only

what is observed in the film, i. e., *Intracellular Gram-negative diplococci resembling gonococci were found*, or, . . . *were not found*. If extracellular Gram-negative cocci resembling the gonococcus are observed, usually a continued search will reveal intracellular groups as well. If, however, only extracellular forms are found, the report should read *Extracellular Gram-negative diplococci suspicious of gonococci were found*, and a request for a second film should be made.

The report should include a statement concerning the number of pus cells present, *Many* . . . *Few* . . . , or *No pus cells present*.

Appendix IV

MEMORANDUM CONCERNING THE USE OF TRYPARSAMIDE

1. This drug is of no value in any form of syphilis except neurosyphilis, and should never be used unless the diagnosis of neurosyphilis has been established by clinical and laboratory methods.
2. In neurosyphilis it should be employed particularly as follows:
   a. As initial treatment in patients with general paresis for whom fever therapy cannot be immediately arranged.
   b. As postfever chemotherapy in general paresis.
   c. In other types of neurosyphilis (excepting those patients with preexisting visual damage), but only when standard antisyphilitic treatment carried on for at least 6 to 12 months has failed to result in clinical improvement and/or improvement in the spinal fluid.
3. The use of tryparsamide is *absolutely contraindicated* in patients with preexisting visual damage, particularly those patients with primary optic atrophy; under no circumstances should it be given to such patients.
4. Tryparsamide is dangerous to vision. About 5 percent of patients treated with it may be expected to develop visual damage which, if the drug is continued, may progress to complete blindness.
5. The drug should never be given to any patient until his eyes have been examined by a competent ophthalmologist. This examination must include opthalmologic examination of the fundi, determination of the corrected visual acuity with the Snellen chart, and an accurately recorded measurement of the peripheral fields for form. If there is constriction of the form fields, even though the fundi and visual acuity are normal, tryparsamide should not be used.
6. The initial symptom of visual damage is the complaint by the patient of blurred, dull or, particularly, "shimmering" vision. The sensation is analogous to that of a normal person sitting behind a hot automobile radiator on a cold day, when waves of hot air rising from the radiator may be seen.
7. Prior to each injection the patient should be questioned as to whether he has any visual symptoms. If he complains of these spontaneously or in response to questioning, the drug should be discontinued immediately and the patient returned to the ophthalmologist for reexamination, particularly of the visual fields. The characteristic constriction of the fields is vertical and there is no scotoma. If the complaint of blurred or shimmering vision is not associated with field constriction, the drug may be cautiously continued, using temporarily smaller doses, and arrangements made for periodic ophthalmic recheck. If, on the other hand, the subjective complaint is associated with field constriction, *the drug must be stopped permanently.*
8. Particular caution should be exercised in the use of tryparsamide in mentally deteriorated paretics who may be unable to cooperate in describing subjective complaints, or in objective opthalmic examination; also in young children.
9. Following the initial pretreatment opthalmic examination, reexamination by the ophthalmologist is not necessary unless there develops subjective visual difficulty.
10. The occurrence of visual reactions may be guarded against to some extent by beginning with an initial dose of 1.0 gram, a second dose of 2.0 grams, and a third and succeeding doses of 3.0 grams each.

11. The average therapeutic dose for an adult weighing 150 pounds is 3 grams. This amount should never be exceeded.
12. The interval between injections should always be one week; never less. The number of injections to the course should be at least 12 and may extend to 25, 50 or even more.
13. In view of the potential gravity of ocular reactions following tryparsamide, the details of any such reaction should be reported promptly to the health department from which the drug was obtained.
14. Failure to observe these precautions may result in complete blindness to the patient and render the attending physician, but not the department of health, liable to medicolegal action.

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Appendix V

MINIMAL CLINIC EQUIPMENT [1]

QUARTERS

1. *Waiting Room*, adequately furnished with chairs for all patients who may gather at any one time, without overcrowding. If space is inadequate for separate waiting rooms for each sex (and where necessary, each race), separate sessions should be held for each. The waiting room should be clean, light, well heated and well ventilated. Reading material should be available to patients who have to wait. Adequate toilet facilities should be available for each sex and (where necessary) each race. The more attractive and comfortable the waiting room, the better case-holding will be. The medical and nursing personnel should try sitting with patients in the waiting rooms of their own clinics as a test of their adequacy and attractiveness.
2. *Examining Room*, adequately equipped for examination of patients for either syphilis or gonorrhea in either male or female.
3. *Intravenous Treatment Room.*
4. *Intramuscular Treatment Room.*
5. *Work Room*, between intravenous and intramuscular treatment rooms, if space is available.
6. *Gonorrhea Treatment Room*, separate rooms for males and females unless the sexes are treated at different sessions.
7. *Private Interview Room*, for either physician or epidemiologist (or social worker) to use as occasion may arise for interview of patient. Initial interview may be had in examining room if complete privacy is assured. If space permits, both physician and epidemiologist (or social worker) should have separate rooms for patient interviews.
8. *Clinic office*, for clerk, records, etc.

Note: The quarters should be so arranged that there is an unobstructed flow of patients from the entrance, through the clinic and to the exit. The flow should not cross itself anywhere, and "detours" for special interviews for special handling should be possible without interfering with the normal clinic flow. Patients should be handled individually, in the examining room, in the treatment rooms, and in case of interview. There should be no standing in line anywhere in the clinic, except as patients enter the clinic and receive their call numbers.

EXAMINING ROOM

SYPHILIS	EITHER OR BOTH	GONORRHEA
	1. Examining table, equipped with stirrups so that pelvic examinations may be made. 2. Linen, cotton or paper sheets for table. 3. Sheets for draping patient. 4. Floor lamp; goose neck, with strong, blue, daylight bulb, at least 75-100 watts. 5. Utility jars; for cotton, gauze, sponges, tongue depressors, applicators.	

[1] Drawn largely from "Manual of Minimum Standards for Cooperating Venereal Disease Clinics," North Carolina State Board of Health. January 3, 1939.

SYPHILIS	EITHER OR BOTH	GONORRHEA
	6. Sponge forceps. 7. Scrub brush, for hands. 8. Soap; liquid preferred, dispensed from a suitable container. 9. Hot and cold running water (lavatory). 10. Towels. 11. Refuse container. 12. Writing table (pen, pencil, ink, forms). 13. Chairs for physician and patient. 14. Thermometer.	
15. Sphygmomanometer (wall type preferred for large clinics). 16. Stethescope. 17. Flashlight. 18. Reflex hammer. 19. Ophthalmoscope (if ophthalmoscopic examinations are to be made). 20. Tuning fork. 21. Measuring tape. 22. Scales for weighing patient.		
	23. Small, medium and large vaginal specula. 24. Rubber gloves.	
		25. Enamel basins (stainless steel is better). 26. Finger cots. 27. Urine glasses (2-glass test). 28. Lubricating jelly; for rectal and prostatic examination. 29. Slides (for Gram stain).
30. Slides (for dark field).		
	31. Serologic outfits. 32. Syringes and needles for collecting blood specimens. 33. Equipment for collecting culture specimens (if culture service available). 34. Alcohol. 35. White coats for physicians.	

Note: If sulfonamide-resistant gonorrhea is to be treated, the above equipment, so far as it pertains to gonorrhea, may be a part of the treatment room equipment and examinations may be made in the treatment rooms.

Laboratory

(For Either Syphilis or Gonorrhea Clinics)

1. Benedict's solution.
2. Acetic acid (1% solution).
3. Urinometer.
4. Centrifuge; for urine sediments.
5. Bunsen burner or alcohol lamp.
6. Solutions for Gram stain.
7. Oil for immersion lens and dark field.
8. Slides and cover slips.
9. Test tubes and test-tube holder.
10. Alcohol.
11. Microscope with low, high dry and oil immersion lenses and dark-field attachment. In large clinics, separate dark-field microscope.
12. Sterilizer.
13. Facilities for preparing cultures (if culture service available).
14. Ice box or electric refrigerator (if blood specimens or cultures must be stored).
15. Hot and cold running water.
16. Soap, towels, etc.
17. Waste receptacle.
18. Work tables, chairs, stools, pen, ink, forms, etc.

Note: In small clinics it may be convenient to have the laboratory in one corner of the examining room.

Lumbar Puncture Equipment

(For Examining Room or Special Lumbar Puncture Room)

Sterile tray containing the following equipment:

1. Two sterile towels.
2. Iodine.
3. Sterile applicators.
4. Novocain (1% solution).
5. Alcohol.
6. Sterile test tubes with sterile cork stoppers.
7. Sterile catheter tray containing the following sterile equipment:
   a. Two No. 22 gauge lumbar puncture needles.
   b. One 2 cc. syringe.
   c. One hypo needle.
   d. One 2″ No. 22 needle (for blood specimen).

Intravenous Treatment Room

1. Treatment table; for patients to lie upon. If space does not permit use of table, patient may be treated sitting in chair with arm resting on a small table.
2. Table for supplies.
3. Drugs to be used.
4. Sterile distilled water in suitable container.
5. Flasks for mixing drugs.
6. Needles, 1½″, 20 to 22 gauge.
7. Syringes, 10 or 20 cc.
8. Syringes, 2 cc.

9. Instrument forceps.
10. Tourniquet.
11. Alcohol.
12. Cotton or gauze.
13. Sterilizer.
14. Chair for operator (and for patient if table is not used).
15. Small table, with pen, ink, forms.
16. Emergency supplies:
    a. Ammonia (aromatic spirits).
    b. Caffein in solution.
    c. Adrenalin.
    d. Morphine tablets.
    e. Sterile hypodermic needles.
    f. Sterile syringe, 2 cc.

Intramuscular Treatment Room

1. Low wooden table, with pad. (Patients should lie on abdomen.)
2. Sheets for table.
3. Small table for equipment.
4. Drugs for intramuscular use.
5. Needles (sterile), 2½", 19 or 20 gauge.
6. Syringes (sterile), 2 or 3 cc.
7. Alcohol.
8. Gauze.
9. Sterilizer.
10. Small table for records, pen and ink.
11. Hooks for patients' hats, coats, etc.

Note: If space is available, it is most convenient to have a workroom between the intravenous and intramuscular treatment rooms, where solutions may be prepared, equipment sterilized, and materials stored in suitable cabinets.

Gonorrhea Treatment Room

[See also, Examining Room]

Male	Either or Both	Female
	1. Treatment (and examining) table, with stirrups if to be used in examination and treatment of women.	
	2. Sheets for table.	3. Sheets for draping female patients.
		4. Floor lamp; goose neck, with strong blue daylight bulb; 75–100 watts.
	5. Utility jars; for cotton, gauze, sponges, applicators.	
		6. Sponge forceps.

MALE	EITHER OR BOTH	FEMALE
	7. Scrub brush, for hands. 8. Soap; liquid preferred, dispensed from suitable container. 9. Hot and cold running water (lavatory). 10. Towels. 11. Refuse container. 12. Writing table; pen, ink, forms. 13. Chair. 14. Stool for physician. 15. Thermometer.	16. Rubber gloves.
17. Finger cots. 18. Valentine irrigator reservoir. 19. Rubber tubing for irrigator, with pinchcock. 20. Rubber meatal tips. 21. Enamel or stainless steel basins. 22. Thermos jugs for irrigant. 23. Urine glasses for two-glass test. 24. Urinal for patient. 25. Sounds for calibrating urethra (and bougies). 26. Rubber catheters.		
		27. Small, medium and large vaginal specula.
	28. Sterilizer. 29. Slides for Gram stain and darkfield. 30. Lubricating jelly for rectal and prostatic examinations. 31. Serologic outfits. 32. Syringes and needles for collecting blood specimens. 33. Equipment for collecting specimens for culture. 34. White coats for physicians.	
		35. Small cubicle, with stool, for patient to disrobe as necessary.
	36. Microscope (unless in laboratory in clinic).	

NOTE: If treatment with sulfonamides only, the equipment for the management of gonorrhea need be only that described under "Examining Room."

Appendix VI

INTERPRETATION OF SPINAL FLUID FINDINGS

Spinal fluid reports should include results of (a) quantitative complement fixation test; (b) total protein or standard globulin test; (c) differential cell count; (d) colloidal test. The fluid should be bloodless. The results of these examinations are to be interpreted as follows:

1. *Minimal abnormality.*
   Slight increase in protein (Pandy doubtful to 1 plus) or lymphocyte count over 5. Continue with standard treatment; recheck at or before probation.
2. *Grade I.*
   Blood positive or negative. Cerebrospinal fluid Wassermann negative. Lymphocyte count 10 to 25. Protein 1 plus. Colloidal test low midzone. Recovers under continuance of standard treatment. Recheck in 6 months.
3. *Grade II.*
   Blood positive or negative; usually positive. Cerebrospinal fluid Wassermann positive in low dilutions; negative in high dilutions. Lymphocyte count 25 to 100 plus. Protein 2 plus. Colloidal test pronounced midzone. Recovers under prolongation and intensification of standard intravenous and intramuscular treatment.
4. *Grade III.*
   Blood strongly positive. Cerebrospinal fluid Wassermann strongly positive in all dilutions. Lymphocyte count 7 to 100 plus. Protein 3 plus. Colloidal test first zone (paretic). Will not recover without tryparsamide and/or fever therapy. Needs expert attention.

Appendix VII

THE PREVENTION AND CONTROL OF REACTIONS TO ANTISYPHILITIC THERAPY

Technical Suggestions

1. Discard discolored drugs and solutions and damaged ampules. Test ampules for minute cracks by immersion in alcohol.
2. Shake and aerate arsenoxide (mapharsen). Never shake nor aerate neoarsphenamine. Inject all other arsenicals slowly; there is danger of speed shock.
3. Inject arsenoxide (mapharsen) rapidly to avoid thrombosis; there is no danger of speed shock.
4. Thoroughly shake oily suspensions.
5. Pull on piston of syringe before injecting anything, especially intramuscularly. Be sure the needle is in the vein for intravenous injections; be sure it is not in a vein or artery for intramuscular injections.
6. Inject intramuscularly into inner angle of upper, outer quadrant of buttock. Fewer large vessels or nerves are to be found in this location and, most important, the patient does not *sit* there! Alternate buttock with every other injection to rest the tissue as long as possible.
7. Massage long and firmly after withdrawing needle from buttock. Have patient prolong massage to 3 minutes.
8. Patient should rest if possible after arsenical injections; exercise after intramuscular injections.
9. Warn patient to report any reactions.
10. Reduce carbohydrates.
11. Test urine once in 2 to 4 weeks if practicable. Do not stop or modify treatment for slight albuminuria or cylindruria.
12. Watch mouth, gums; use peroxide or other oxidant, and an astringent if available. Dental attention if available.

General Antireaction Therapy

1. Adrenalin solution 1:1,000, minims VI to X, subcutaneously, for speed shock or nitritoid crises.
2. Glucose intravenously for jaundice or dermatitis.
3. Venesection, 400 cc., for threatened cerebral accidents.
4. Liver extract intramuscularly is occasionally helpful in suspected liver damage.
5. In cerebral vascular accidents, hypertonic saline intravenously.
6. In blood dyscrasias, transfusions.
7. The value of sodium thiosulfate for any type of treatment reaction is questionable.
8. WHEN IN DOUBT, ASK THE ADVICE OF AN EXPERT CONSULTANT.

Appendix VIII

THE PROPHYLAXIS OF SYPHILIS AND GONORRHEA

Chemical Prophylaxis

This is really early treatment applied before the organisms have had time to penetrate the tissues. It can prevent infection with all venereal diseases if properly applied and if used early enough. It is most effective if applied within an hour after exposure (the first exposure of the series, not the last), and rapidly decreases in value as the interval between exposures and treatment lengthens. It is still of some value, especially against syphilis, as late as 8 hours after exposure.

Under conditions of military control, especially in our own Army and Navy, chemical prophylaxis has been brilliantly successful in reducing the incidence of venereal disease to a remarkably low level. Unfortunately, in civilian life it is practically unworkable since men will not take it except under compulsion. Nevertheless, every physician should know the steps in the technic.

Technic of prophylaxis for the male.—If possible do not allow the patient to administer the treatment to himself. The patient is made to urinate. He is provided with a basin of warm water and a gauze wipe, with which he washes the genitals thoroughly while liquid green soap is dropped on the penis. The washing to be done thoroughly should consume about 10 minutes and should include the penis, scrotum, pubis, and the adjacent areas of the thighs. Use especial care to wash thoroughly the folds of the frenum and foreskin. After washing, the parts should be dried thoroughly. The washing with soap and water is important; soap is the only part of the treatment effective against chancroid, and is also of value as a destroyer of the organism of syphilis. Before proceeding further the presence of urethral discharge or genital sores is noted.

The next step is the injection of 1 dram (4 cc) of a freshly made 2 percent protargol solution (or a 10 percent solution of argyrol) into the urethra by the physician. The patient then holds the meatus firmly between the thumb and forefinger for 5 minutes, from time to time allowing a drop to escape from the meatus so that all parts of the urethra are in contact with the solution. At the end of 5 minutes the protargol is allowed to escape, without pressure or stripping, so that a few drops remain. One-half to 1 dram (2 to 4 grams) of 33 percent calomel ointment is next rubbed thoroughly by the patient, under the observation of the physician, into all parts of the penis for 5 minutes, special attention being paid to the retracted prepuce, the frenum, and the glans. The scrotum also should be rubbed with ointment. The genitalia are then wrapped in toilet paper or waxed paper to protect the clothes, and the patient is instructed not to urinate for four or five hours.

The formulae for calomel ointment used in the United States Army and Navy, which have proved their efficacy, are as follows:

United States Army	*Parts*
Hydrargyri chloridum mite	30
Adeps benzoinatus	65
Cera alba U. S. P.	5

United States Navy	*Parts*
Calomel	33
Camphor	2
Phenol	3
Anhyd. lanolin	39
Benz. lard	20
Beeswax	3

Remember that soap and water is protection against chancroid and partially against syphilis, protargol against gonorrhea, and calomel ointment probably only against syphilis.

Before and since the war an extensive search has been made for one drug or a combination which might prove effective against all three diseases, but so far without satisfactory results.

If prophylactic treatment under the direction of a physician is not available, it is worth while for the patient to be advised to use one of the individual prophylactic packets put out by various commercial houses, directions for the use of which usually accompany the packet. Though this is not as satisfactory as the scheme outlined above, the experience of the United States Navy and the Australian and New Zealand troops during the war indicate that it is of some value; and the prevention of only a single case of syphilis is a worth-while accomplishment.

Technic of prophylaxis for the female.—In cases of rape, and in some others, there may be occasion for applying early treatment to females. If such occasion should arise, the following procedure is suggested: Have the patient urinate. Place the patient in the lithotomy position. Wash the genitals and adjacent parts with soap and water. Give a douche of 2 quarts of sterile water, temperature 100° F., followed by 2 quarts of 1:2000 mercuric chloride solution, and wash external parts with the latter. Dry the vagina and vulva by sponging. Swab the entire vagina, through a speculum, with a 2 percent protargol solution, or 10 percent argyrol solution, freshly made; reach every fold and especially the posterior vault and external os. Swab the entire vulva in the same way, reaching every recess. Inject enough of the same solution into the urethra to distend it moderately and let the patient hold her finger (in a rubber glove) against the meatus to retain the solution for from 3 to 5 minutes.

Douche the vagina and vulva with a small amount of sterile water, and sponge dry with gauze. Apply calomel ointment to the cervix, vagina, vulva and adjacent parts, rubbing thoroughly into the recesses and folds of the mucous membranes and skin, and taking at least 10 minutes for the operation. Do not use more than 4 grams (1 dram) of calomel ointment in the vagina. Cover the external parts securely with oiled silk or waxed paper, and instruct the patient to allow ointment to remain for several hours before washing the parts.

The civilian substitute for the Army technic is the prophylactic tube, of which several varieties are on general sale. All of them depend on the incorporation in a single ointment base, dispensed in a collapsible tube, of a combination of chemicals supposedly effective against both gonorrhea and syphilis. Although the user of this tube may not dispense with the preliminary thorough washing with soap and water (which is probably as effective against syphilis as calomel ointment) and although phenol and the silver salts in an ointment base are not as efficient against gonorrhea as an aqueous solution, such tubes may do some good in prevention. Their sale should be encouraged, and research efforts to improve them continued.

Chemical prophylaxis has, however, a highly important place in the prevention of accidental infection with syphilis among doctors, nurses, and dentists. In the ordinary handling of infectious lesions, even if there are abrasions on the fingers, immediate thorough washing with soap and water is adequate protection. In the case of scratch or puncture wounds with infected instruments, the wound should be laid open with a sterile scalpel to the approximate depth of the puncture, and should be packed with 33 percent calomel ointment, which is allowed to stay in place for 24 hours under a sterile dressing.

Chemotherapeutic Prophylaxis

Three methods are advocated: (1) The oral use of stovarsol (synonyms, acetarsone, spirocid), a pentavalent arsenical, both before and after exposure; (2) frequently repeated intramuscular injections of bismuth during the active period when exposures may be expected to occur; (3) the intravenous injection of an arsphenamine after exposure.

Stovarsol may be dismissed from present consideration because the case for it is not yet proved, and because the drug is too toxic.

Bismuth prophylaxis, applicable to groups of prostitutes, is obviously useless in ordinary practice, since it is tantamount to the continuous antisyphilitic treatment of noninfected persons.

The proposals for arsphenamine prophylaxis are so far limited to those individuals exposed to a known infectious syphilitic. If this somewhat unusual situation arises, and if one or several injections of arsphenamine can be given within 48 (preferably 24 hours) after exposure, it is claimed that the development of syphilis may be prevented. While this is true in the experimental animal, the value of the procedure in man is still debatable. It is open to the objection that if it is carried out, the infection may be only suppressed instead of eradicated. In any case, both physician and patient are in the difficult position of not knowing whether or not the patient would have acquired the disease if not so treated. On the other hand, it is probable that under these circumstances, if infection actually has occurred, it may be "cured" with more certainty and with less treatment than if one waits for lesions or a positive blood serologic test to appear. On the whole, the controversy between the advocates and opponents of this plan may be compromised by putting the question squarely up to the patient as follows: "Since you have been exposed to a known infectious syphilitic, it is probable though not certain that you have acquired the disease. If you have acquired it, it can be 'cured' more easily and with less treatment if you start immediately than if you wait for lesions to appear. But, if you take treatment now, you must regard yourself as a syphilitic, and though you have been more fortunate than most in that your treatment was begun very early, you must be followed for a lifetime of observation, exactly as if you had developed lesions."

If the patient chooses early prophylactic treatment, (1) it should not be given later than 48 hours after the suspected exposure; (2) it should consist, not of one or two arsphenamine injections, but of at least one complete arsphenamine course (8 arsphenamine or 10 neoarsphenamine or silver-arsphenamine), followed by a course of bismuth or mercury; (3) the patient should be followed with monthly blood serologic tests for the first year, every 2 or 3 months for the second year, and thereafter every 6 to 12 months for 2 or 3 years, and must have at least one negative spinal fluid examination at the end of the first year of observation. This is essential to guard against the possibility that the infection has been only suppressed, instead of eradicated, with the resultant likelihood of visceral, cardiovascular, or neurosyphilis in the future. If the patient is unwilling to subscribe to all of the above, especially the probationary follow-up, it is far better to withhold prophylactic arsphenamine and to observe him closely for the appearance of lesions or the development of a positive blood serologic test before treatment.

Mechanical Prophylaxis

Since neither chemical nor chemotherapeutic prophylaxis is at present suitable for widespread application in practice, the main hope of prevention of syphilis and other venereal diseases is mechanical prophylaxis, the condom. This is a method which is simple, painless, inexpensive, affords protection against all of the venereal diseases and to both sexes at once, and which, applicable before and during the act of intercourse,

eliminates the psychologic hazards associated with the other methods. Its chief drawbacks at present are the poor quality of some of the condoms available on the market, the refusal of some types of individuals to use them, the ignorance of others as to their effective use, and the possibility of infection with syphilis on areas not covered by the condom.

In the interest of prevention of venereal disease, physicians generally should lend support to efforts to improve methods of manufacture and distribution of condoms, and should foster dissemination of information concerning their use. If every illicit sexual contact were protected by this means, venereal diseases would immediately diminish.

Appendix IX

THE MAY ACT

The May Bill: (Public Law 163—77th Congress; Chapter 287—1st Session; H. R. 2475.—Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That until May 15, 1945, it shall be unlawful, within such reasonable distance of any military or naval camp, station, fort, post, yard, base, cantonment, training or mobilization place as the Secretaries of War and/or Navy shall determine to be needful to the efficiency, health, and welfare of the Army and/or Navy, and shall designate and publish in general orders or bulletins, to engage in prostitution or to aid or abet prostitution or to procure or solicit for the purposes of prostitution, or to keep or set up a house of ill fame, brothel, or bawdy house, or to receive any person for purposes of lewdness, assignation, or prostitution into any vehicle, conveyance, place, structure, or building, or to permit any person to remain for the purpose of lewdness, assignation, or prostitution in any vehicle, conveyance, place, structure, or building or to lease, or rent, or contract to lease or rent any vehicle, conveyance, place, structure, or building, or part thereof, knowing or with good reason to know that it is intended to be used for any of the purposes herein prohibited; and any person, corporation, partnership, or association violating the provisions of this Act shall, unless otherwise punishable under the Articles of War or the Articles for the Government of the Navy, be deemed guilty of a misdemeanor and be punished by a fine of not more than $1,000, or by imprisonment for not more than one year, or by both such fine and imprisonment, and any person subject to military or naval law violating this Act shall be punished as provided by the Articles of War or the Articles for the Government of the Navy, and the Secretaries of War and of the Navy and the Federal Security Administrator are each hereby authorized and directed to take such steps as they deem necessary to suppress and prevent the violation thereof, and to accept the cooperation of the authorities of States and their counties, districts, and other political subdivisions in carrying out the purposes of this Act: *Provided*, That nothing in this Act shall be construed as conferring on the personnel of the War or Navy Department or the Federal Security Agency any authority to make criminal investigations, searches, seizures, or arrest of civilians charged with violations of this Act. Approved, July 11, 1941.

Appendix X

AN AGREEMENT

By the War and Navy Departments, the Federal Security Agency, and State Health Departments on Measures for the Control of the Venereal Diseases in Areas Where Armed Forces or National Defense Employees are Concentrated [1]

It is recognized that the following services should be developed by State and local health and police authorities in cooperation with the Medical Corps of the United States Army, the Bureau of Medicine and Surgery of the United States Navy, the United States Public Health Service, and interested voluntary organizations:

1. Early diagnosis and adequate treatment by the Army and the Navy of enlisted personnel infected with the venereal diseases.

2. Early diagnosis and treatment of the civilian population by the local health department.

3. When authentic information can be obtained as to the probable source of venereal disease infection of military or naval personnel,[2] the facts will be reported by medical officers of the Army or Navy to the State or local health authorities as may be required. If additional authentic information is available as to extramarital contacts with diseased military or naval personnel during the communicable stage, this should also be reported.

4. All contacts of enlisted men with infected civilians to be reported to the medical officers in charge of the Army and Navy by the local or State health authorities.

5. Recalcitrant infected persons with communicable syphilis or gonorrhea to be forcibly isolated during the period of communicability; in civilian populations, it is the duty of the local health authorities to obtain the assistance of the local police authorities in enforcing such isolation.

6. Decrease as far as possible the opportunities for contacts with infected persons. The local police department is responsible for the repression of commercialized and clandestine prostitution. The local health departments, the State Health Department, the Public Health Service, the Army, and the Navy will cooperate with the local police authorities in repressing prostitution.

7. An aggressive program of education both among enlisted personnel and the civilian population regarding the dangers of the venereal diseases, the methods for preventing these infections, and the steps which should be taken if a person suspects that he is infected.

8. The local police and health authorities, the State Department of Health, the Public Health Service, the Army, and the Navy desire the assistance of representatives of the American Social Hygiene Association or affiliated social hygiene societies or other voluntary welfare organizations or groups in developing and stimulating public support for the above measures.

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[1] Adopted by the Conference of State and Territorial Health Officers, May 7–13, 1940.

[2] Familial contacts with naval patients will not be reported.

Appendix XI

SUGGESTED READING LIST

This reading list by no means covers the important literature on the management and control of gonorrhea and syphilis. It includes the more recent and especially useful documents with which every venereal disease control officer should be intimately familiar. (See also Reference, p. 79.)

1. Supplements to Venereal Disease Information:
   No. 5. The Diagnosis of Syphilis by the General Practitioner.
   No. 6. Management of Syphilis in General Practice.
   No. 7. Syphilis in Mother and Child.
   No. 8. Report of the Committee for Survey of Research on the Gonococcus and Gonococcal Infections.
   No. 9. The Serodiagnosis of Syphilis.
      Pt. 1. Proceedings Assembly of Laboratory Directors and Serologists.
      Pt. 2. Revised Technics of the Eagle, Hinton, Kahn, Kline, and Kolmer Tests.
   No. 10. Control of Venereal Diseases in the United States. Present and Future Plans.
   No. 11. Technics of Serodiagnostic Tests for Syphilis.
   No. 12. Conference on Venereal Disease Control.
   No. 13. The Newer Chemotherapy of Venereal Diseases.
   No. 14. Modern Serologic Tests for Syphilis.
2. Conference of State and Territorial Health Officers, May 1–2, 1941. Plans for Venereal Disease Control. Ven. Dis. Inform., **22**: 233–236, 1941.
3. Directory of Venereal Disease Clinics. Supp. No. 4 to Ven. Dis. Inform. Issued annually by the U. S. Public Health Service. (Each clinic should have a copy to facilitate transfer of patients to treatment elsewhere and for request for treatment records of patients previously treated elsewhere.)
4. The Gonococcus and Gonococcal Infection. Publication No. 11, American Assoc. Advance. Sc., New York, The Science Press, 1939.
5. Hazen, H. H., and others: The Chemical and Mechanical Prevention of Syphilis and Gonorrhea. Preliminary statement by the special joint committee appointed by the American Social Hygiene Association and the U. S. Public Health Service. Ven. Dis. Inform., **21**: 311–313, 1940. Also issued as Reprint No. 138 from Ven. Dis. Inform.
6. Moore, J. E.: The Modern Treatment of Syphilis, 2d ed. Baltimore and Springfield, Charles C. Thomas, 1941.
7. Nelson, N. A.; Crain, G. L.: Syphilis, Gonorrhea and Public Health. New York, The Macmillan Co., 1938.
8. Pelouze, P. S.: Gonorrhea in the Male and Female, 3d ed. Philadelphia, W. B. Saunders Co., 1941.
9. Stokes, J. H.: Modern Clinical Syphilology, 2d ed. Philadelphia, W. B. Saunders Co., 1936.
10. Venereal Disease Information.[1]

[1] Every venereal disease control officer, every clinic physician, and every physician who treats the venereal diseases in private, hospital or other institutional practice should regularly subscribe to and read this publication issued monthly by the U. S. Public Health Service. It carries not only important original articles, but also abstracts of articles appearing in current periodicals. (N. A. N.)

Acetarsone

in the Treatment of Congenital Syphilis

A REVIEW OF THE LITERATURE

Josephine Hinrichsen, M. S., M. D.

Supplement No. 18

To Venereal Disease Information

FEDERAL SECURITY AGENCY

U. S. PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

United States
Government Printing Office
Washington : 1942

For sale by the Superintendent of Documents, Washington, D. C. - - Price 15 cents

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ACETARSONE IN THE TREATMENT OF CONGENITAL SYPHILIS

A Review of the Literature

JOSEPHINE HINRICHSEN, M. S., M. D.

THE CHIEF purpose of this study of the literature is to evaluate the role of acetarsone in the treatment of congenital syphilis. The experimental studies of this drug in animals, its toxic effects in adults, and its therapeutic effect in adult syphilis, particularly primary and secondary syphilis, are reviewed in considerable detail because of the direct relationship they bear to the problem of treatment of congenital syphilis. In regard to treatment, primary and secondary syphilis are comparable to early congenital syphilis with manifestations. In recent years early manifestations of congenital syphilis have become less frequent because more pregnant women are being treated. For that reason, the diagnosis of early congenital syphilis and therefore also the evaluation of treatment results are more difficult. If the infant did not actually have syphilis, yet received treatment because this fact was obscured, the antisyphilitic treatment given, of course, would result in negative findings in regard to syphilis. This applies particularly to infants to whom acetarsone is given because of the finding of a positive serologic reaction in the mother, that is, without establishing the diagnosis of congenital syphilis in the infants themselves.

HISTORY OF THE DRUG

Acetarsone (stovarsol), which is acetylaminohydroxyphenylarsonic acid [1] ($HO.CH_3CONH.C_6H_3.As:O:(OH)_2$), the acetyl derivative of 3-amino-4-hydroxyphenyl-1-arsonic acid, first appeared in New and Nonofficial Remedies in January 1926. It is a white, odorless powder, having a slightly acid taste. It is slightly soluble in water and alcohol, and readily soluble in solutions of alkalis or alkaline carbonates. It is stable at ordinary temperatures and contains from 27.1 to 27.4 percent of arsenic. In different countries it is known under various names, such as stovarsol (France),

[1] According to American terminology, an arsonic acid is an organic compound derived from pentavalent arsenic, e. g., $R\text{-}AsO(OH)_2$, a monosubstituted arsenic acid, whereas an arsinic acid is a compound derived from pentavalent arsenic which contains two, similar or different, organic groups, e. g., RR-AsO(OH). Since acetarsone is a derivative of pentavalent arsenic and represents a monosubstituted arsenic acid, it is accordingly termed "acetyl-amino-hydroxy-phenylarsonic acid." In European literature, however, this differentiation between arsonic and arsinic is not made, all of the compounds of this type being referred to as arsinic acids (*32*).

spirozid or spirocid (Germany), stovarsolan or osarsol (Russia), paroxil (Spain and South America). Other less common names for this drug, according to Fischl and Schlossberger (*60*) are goyl, karophen, orarsan, and osvarsan. These authors and also Burke (*25*) further emphasized that the name "acetarsone" and its synonyms indicate the free acid and not the monosodium salt (some authors have incorrectly referred to acetarsone as the sodium salt of acetylaminohydroxyphenylarsonic acid). Fischl and Schlossberger also made an interesting comment on the possible origin of the term "stovarsol." They pointed out that the French word "fourneau" translated into English means "stove." According to numerous reports in the literature, this compound was first prepared by Ehrlich, it being number 594 of his series. However, no reference to it can be found in the monograph by Ehrlich and Hata (*52*) on chemotherapy. Bertheim (*15*) in 1908 described a method for preparing aminophenylarsinic acid, and Ehrlich and Hata in their monograph published in 1910 reported that mice treated with dichlorphenylarsinic acid as well as with aminophenylarsinic acid develop 2 weeks after treatment a disturbance of the nervous system characterized by chronic tremor of the head and neck and that these mice finally become dancing mice. Levaditi (*114*) stated that although acetarsone was first prepared by Ehrlich he did not systematically examine it, that it was one of a series of arsenical compounds known as "arsinic acids" in which the arsenic is pentavalent, and Ehrlich considered the members of this series to be considerably inferior to the "arsenobenzenes" in which the arsenic is trivalent. Kolle (*98*) reported in 1924 that Ehrlich's original preparation "594" (found to be identical with stovarsol) was still in stock at the Georg-Speyer Haus. According to Pinkus (*163*), acetarsone was one of a series of phenylarsinic acids prepared by Ehrlich and Hata and used subcutaneously. They did not try the oral administration of this drug.

In 1921, Fourneau (*61*) at the Institut Pasteur decided to reinvestigate the arsinic acids, believing the unsatisfactory results obtained by Ehrlich to be directly attributable to the presence of impurities. Fourneau and his coworkers, M. and Mme. Tréfouel, prepared them and tested them on both animals and human beings, using both the intramuscular and subcutaneous modes of administration. Fourneau, Navarro-Martin and M. and Mme. Tréfouel (*62*) in their detailed report on the study of the phenylarsinic acids stated that the peroral effective curative dose, as well as the toxic dose, is very difficult to determine but that it does not seem to be higher than that to be used for subcutaneous injection. According to them the elimination of arsenic in the urine showed that stovarsol is absorbed rapidly and in considerable quantity from the digestive tract. Tests were carried out with amino-oxy-phenylarsinic acid ("189") and acetyloxyaminophenylarsinic acid ("190"-"stovarsol") in experimental syphilis by

Levaditi and Navarro-Martin and in human syphilis by Fournier, Guenot and Schwartz (*116*).

In their first experiments which were carried out on 4 rabbits with lesions of experimental syphilis, stovarsol was administered subcutaneously. In 1 rabbit which received 0.2 gm. per kg. of body weight the treponemes disappeared from the lesions on the day following the injection, and the lesion healed rapidly. Rabbits 2, 3, and 4 received respectively 0.1 gm., 0.05 gm., and 0.01 gm. per kg. of body weight, and it was found that in these dosages treponemes were not destroyed and the lesions did not heal.

At the time these studies with stovarsol were being carried out, Sazerac and Levaditi (*114*) were investigating the prophylaxis of syphilis by means of soluble bismuth salts administered by mouth. Since the experiments with bismuth did not give very encouraging results, Levaditi and Navarro-Martin decided to determine the effect of stovarsol administered by mouth. Both the prophylactic and the curative action of this substance were studied.

In reports by Levaditi and Navarro-Martin (*117*, *118*) and by Levaditi, Navarro-Martin, Fournier, Guenot and Schwartz (*64*, *116*), Levaditi and Navarro-Martin showed by means of results obtained on 21 rabbits that stovarsol administered perorally 2 hours, 5 hours, 6 hours, 12 hours, 24 hours, 2 days, and even 7 days after experimental syphilis infection was prophylactically effective. The minimum effective single dose was 0.1 gm. per kg. (2 rabbits), the other doses varying from 0.16 gm. to 0.7 gm. per kg. The dose of all except 2 rabbits did not exceed 0.35 gm. per kg.; these 2 received 0.7 gm. per kg. Twenty of the rabbits received single doses, and only 1 received 2 doses (2 x 0.7 gm. per kg.). The animals were observed for from 24 to 76 days, and only 1 of them developed lesions. These lesions appeared 75 days after treatment. All of the controls developed syphilitic lesions. The prophylactic efficacy of stovarsol was found to be equally good in 10 rabbits which, instead of being inoculated with syphilitic material, were exposed to the infection by sexual contact with rabbits having syphilitic lesions. On the day after exposure they received stovarsol in doses of from 0.1 to 0.15 gm. per kg. and were observed for from 35 to 75 days. All of the controls but none of the treated animals became infected.

In these same publications Levaditi and his coworkers reported on the prophylactic effect of stovarsol in 2 men and 9 women (*113*). The men, who were, respectively, 32 years old (with negative history for syphilis and negative blood Wassermann reaction) and 25 years old (no statement made in regard to previous infection or blood Wassermann reaction), permitted themselves to be inoculated with syphilitic material on both arms by means of scarification. The same syphilitic material was simultaneously inoculated into the eyebrows of a Macacus cynomolgus monkey, one monkey being inoculated for each patient. The first man received 2 gm.

of stovarsol by mouth 5 hours after inoculation, and the second man received 2 gm. of stovarsol by mouth 2½ hours and again 16 hours after scarification (total 4 gm.). One of the monkeys developed syphilitic lesions 10 days and the other 11 days after inoculation. The first man was observed for 68 days, and his blood Wassermann reaction was negative on the fifty-first day; the second man remained free from lesions and serologically negative for 47 days of observation. A total of 9 women who had been sexually exposed to husbands with chancres were given prophylactic treatment with stovarsol. The dose was 1 to 1.5 gm. daily, given every day or every 2 days and usually in courses of 3 to 4 days separated by rest periods of a few days to a week. Most of the women received 2 or 3 such courses. The total dosage varied from 4.0 to 11.0 gm., administered in a period of from 4 to 17 days. The length of the observation period is given for only 3 women, it being 1½, 1¾, and 3½ months, respectively, at the end of which time they were free from symptoms, and the blood Wassermann reaction was negative. The statement is made for all of them, however, that stovarsol prophylaxis was successful.

The curative properties of stovarsol in experimental and in human syphilis were studied by Levaditi, Navarro-Martin, Fournier, Guenot and Schwartz (*116*). The experimental studies were carried out on 3 rabbits and 1 Macacus cynomolgus, all of which had syphilitic lesions containing numerous treponemes. A 10-percent solution of the sodium salt of acetyloxyaminophenylarsonic acid was administered by mouth. Rabbit 1 received a dose of 2 gm. This resulted in the disappearance of treponemes from the lesions on the second day, at which time another 2 gm. dose was given. With this total dose of 4 gm. (1.5 gm. per kg. of body weight) the lesions healed by the fourth day and the spirochetes definitely disappeared. Rabbit 2, which received only a single dose of 2 gm. (0.66 gm. per kg.), showed complete healing of the lesions by the eighth day. The spirochetes disappeared from the lesions on the first day. Rabbit 3 had lesions containing Spirochaeta cuniculi. A single dose of 1 gm. (0.3 gm. per kg.) resulted in cure of the lesion by the third day with no recurrence. The Macacus cynomolgus 12 days after the onset of lesions in the eyebrows received 1.5 gm. of stovarsol and on the third day another dose of 1 gm. Spirochetes disappeared on the third day and definite cure occurred on the sixth day.

In discussing these experiments the authors stated that stovarsol is toxic per os in a dosage of 0.66 gm. per kg. of body weight, the rabbits dying on the 19th to 24th day after its administration, but that it is well tolerated in a dose not exceeding 0.3 gm. or 0.4 gm. per kg. They stated that the therapeutic dose per os, although difficult to establish in a definite manner, is similar to that which has been found for the subcutaneous route. They found the toxic dose for the rabbit by subcutaneous administration to be 0.5 gm. per kg. of body weight. Based on these findings and on the study

of elimination of arsenic in the urine in men and the animal as carried out by M. and Mme. Tréfouel, these authors concluded that stovarsol is rapidly absorbed and in considerable quantity from the digestive mucosa.

The curative effect of stovarsol was studied in 80 patients with syphilis (30 with primary, 42 with secondary, and 8 with tertiary lesions). The sodium salt which was first used was later completely replaced by the acid (stovarsol). The dosage was 1 gm. a day for 5 to 7 days followed by a rest period of equal duration so that a total dosage of 12 to 16 gm. was given in the first month. The daily dosage of 1 gm. was taken before breakfast. Some of the patients received 1 gm. every 2 days for 1 week followed by a rest period of 3 to 4 days and then further treatment. It was observed that the spirochetes disappeared from the surface of the lesions in 24 to 48 hours. Cicatrization of the chancre occurred in from 5 to 15 days, the roseola disappeared after several days of treatment, papular and hypertrophic lesions showed improvement after the first week, and gummas cicatrized in 1 month. There were, however, some exceptions to this rapid action of the drug. In 2 patients with chancres the spirochetes did not disappear after 6 and 8 days of treatment, and the lesions showed no tendency to heal. These patients responded well to bismuth therapy. In 2 cases with roseola and papules the lesions were little influenced; the results were also poor in a patient with gumma of the sternum and in a case of iritis.

The authors stated that in spite of the fact that the superficial cicatrization caused by stovarsol is as rapid and effective as that produced with other drugs, its deep action was often mediocre. In 4 cases secondary lesions recurred 1 or 2 weeks after the first course of treatment; in 6 cases a recurrence was observed at the end of 1 or 2 months. They also observed 1 case of neurorecurrence (facial paralysis) and 1 case of recurrent secondaries with icterus.

The blood serologic reaction for syphilis became negative in only 10 (12.5 percent) of the patients treated with stovarsol. In these the therapeutic results were considered satisfactory although the authors stated that these could not be considered to be definite cures. They concluded from this study that the deep action of stovarsol is more variable and uncertain than that of other arsenicals and suggested that perhaps the dosage would have to be increased or the drug administered by another than the oral route. Because of this uncertain curative effect they advised that stovarsol be used in combination with bismuth therapy, especially in cases in which intravenous injections are impracticable.

It was only natural that the reports of the French investigators should arouse interest in Germany and lead to chemical and experimental comparative studies of stovarsol and Ehrlich's preparation "594." Inquiries at the Georg Speyer-Haus revealed that some of the original preparation of acetylaminohydroxyphenylarsinic acid was still in stock and that it had been

investigated under the number 594. Chemical studies of this original preparation were now made and it was found to be crystalline and chemically pure. It was also found to have exactly the same action against trypanosomiasis as Fourneau's stovarsol (*98*). Kolle in discussing Worm's paper (*216*), therefore, pointed out that Fourneau's claim that he was the first to prepare a pure stovarsol is unwarranted.

The animal experiments which were carried out first in Germany and later in other countries, chiefly in the United States, in order to determine the toxicity and the prophylactic and curative action of acetarsone shall now be considered.

EXPERIMENTAL STUDIES

Toxicity Experiments

Kolle (*98*, *99*) found the toxicity of stovarsol to be much greater than that reported by Levaditi (who performed very few animal experiments). On the basis of the findings in large series of experiments carried out in the Speyer-Haus, Kolle reported that rabbits are not able to tolerate 0.3 to 0.4 gm. per kilogram, as Levaditi reported, but that they died after a dosage of 0.1 gm. per kilogram of stovarsol and that the tolerated dose by mouth varied between 0.05 and 0.07 gm. per kilogram. Stovarsol was found to be less toxic when administered subcutaneously or intravenously, 0.3 gm. per kilogram being the toxic and 0.2 gm. per kilogram the tolerated dose when given subcutaneously and 0.4 gm. per kilogram being the toxic and 0.3 gm. per kilogram the tolerated dose when given intravenously. Because he found the toxicity of stovarsol to be greater when administered by mouth, Kolle assumed that the drug is changed either in the intestinal wall during absorption, or in the liver. He assumed that a reduction process occurred whereby the arsinic acid was reduced to an arsenoxide. The fact that stovarsol is effective in smaller doses when given by mouth than when administered subcutaneously or intravenously would support the correctness of this assumption. Kolle thought that the continued slow absorption of small amounts from the intestine also played a role and that the toxic action after peroral administration may also be due to the splitting off of small amounts of inorganic arsenic.

Worms, (*217*, *218*) at the Reichsgesundheitsamt, carried out special toxicity experiments using the original preparation of stovarsol and spirocid ("594") on 6 rabbits; 3 of these received 0.7, 0.9, and 1.5 gm. per kilogram respectively of stovarsol by peroral administration. The animal which had received 0.7 gm. per kilogram became seriously ill but survived, the animal which had received 0.9 gm. per kilogram died after 6 days, and the one which had received 1.5 gm. per kilogram was killed on the fourth day for the purpose of histologic study. With the peroral administration of spirocid,

dosages of 0.7, 0.9, and 1.0 gm. per kilogram resulted in death of the rabbits in 14, 10, and 4 days, respectively. In the group of rabbits used for therapeutic and prophylactic experiments, 25 out of the total of 64 (39 percent) died from the toxic effects of the preparations (comparative studies were made with spirocid and stovarsol). Deaths from intercurrent infections were not included in these figures. In order to obtain comparable conditions for the evaluation of this preparation for man, Worms tried to determine whether the maximal doses for man of 1 to 2 gm. per day (about 0.017 to 0.033 gm. per kilogram) would have a prophylactic and therapeutic effect in rabbits when these amounts are given at intervals of 1 to 2 days, as the drug is administered to the human being. But even with this dosage deaths due to the toxic action of the drug occurred among the animals, and this dosage was often ineffective therapeutically and prophylactically. According to Worms the toxic action of the drug in the rabbit manifests itself by initial loss of weight which may be transitory or which may lead to death. The effect of the drug seemed to be one of slow, insidious poisoning. Worms therefore cautioned that the drug should be used with great care in the treatment of human beings. Worms concluded that because individual variation in the susceptibility of rabbits to the drug is so great, it is impossible to determine with certainty a nontoxic active dose for the rabbit and that it is possible but unlikely that conditions in the human being are better when the results of these experiments are taken into consideration.

Kritschewsky and Rosenholz (*102*) considered the rabbit as an unsuitable animal for the study of the action of acetarsone. Using the white mouse they found on subcutaneous injection of a 10-percent solution of stovarsolan (Russian preparation) that the maximum tolerated dose was 0.040 gm. per 20 gm. of body weight and the toxic dose 0.050 gm. per 20 gm. of body weight. When administered by mouth the maximum tolerated dose was 0.100 and the toxic dose 0.115 gm. per 20 gm. of body weight. Severe damage of the central nervous system was observed with low as well as high dosage in some animals, although high dosage more often produced injury.

Ewins and Everett (*54*) examined a series of organic arsenic derivatives for toxicity and for their curative action against Trypanosoma equiperdum, by oral as well as other modes of administration. They found the peroral toxic dose of stovarsol for the mouse to be 0.090 gm. per 20 gm. (4.5 mg. per gm.).

Collier and Evers (*36*) at the Speyer-Haus also carried out toxicity experiments. Their results, obtained on 48 rabbits, also did not agree with those of Levaditi and coworkers. Even the small dose of 0.05 gm. of stovarsol per kilogram was not well tolerated. Out of 5 rabbits which received this dosage, only 2 survived. Among 8 rabbits which received a dose of 0.1 gm. per kilogram and 8 others which received 0.2 gm. per kilogram,

only 1 in each group survived. All of the other 27 animals which received 0.3 gm. per kilogram and higher doses died. The results of Schlossberger's toxicity determinations with the original Ehrlich preparation, 594, which he also carried out at the Speyer-Haus are included in this report by Collier and Evers. He found 594 to be exactly identical with Fourneau's stovarsol. All of the animals which received 594 (0.1, 0.2, 0.3, and 0.4 gm. per kilogram) died.

Poole (*164*) carried out toxicity experiments on 14 rabbits. The original French stovarsol furnished by Fourneau was used. Each of the following amounts was given to each of 2 rabbits: 1.0, 0.75, 0.6, 0.5, 0.4, 0.3, and 0.2 gm. per kilogram. Twelve rabbits died within 20 days after treatment, the 2 surviving rabbits having received 0.6 and 0.3 gm. per kilogram of stovarsol respectively. In general, those receiving larger doses died earlier than those receiving smaller doses. Poole pointed out that his experiments did not disclose the minimum lethal dose nor the maximum tolerated dose but that his findings agreed with those of Kolle. There was little doubt that death in the rabbits was due to stovarsol poisoning. The first symptom noted was anorexia followed by lethargy. A few days before death profuse watery diarrhea was noted. There was no evidence of blindness.

Takatsu (*202*) administered spirocid perorally to 7 rabbits with syphilitic orchitis. The single dose of 0.05–0.1 gm. per kilogram was repeated on the next 2 days so that a total dose of 0.2–0.3 gm. per kilogram was given. Four of the rabbits died from drug intoxication after an interval of 11 to 23 days.

Frazer (*65*), who studied the effect of various organic arsenic compounds on experimental Spirillum minus infections of rats and guinea pigs also studied the action of stovarsol. This drug was given to rats only and was administered perorally. The minimum lethal dose was not found. The largest amount given was 0.8 gm. per kilogram administered over a period of 3 days. No ill-effects were observed following this dosage; the animal did not even lose weight.

Anderson and Leake (*3*) studied the toxicity of acetarsone and its calcium and sodium salts on peroral administration to 35 cats and 56 rabbits. They found the minimal lethal dose of commercially available acetarsone for these animals to be between 0.125 and 0.175 gm. per kilogram. The minimal lethal dose of the calcium and sodium salts of acetarsone on peroral administration to cats and rabbits was found to be about the same as that of acetarsone itself. This finding is in agreement with that of Collier and Evers (*36*) who on the basis of experiments on 4 rabbits found that suspension of stovarsol in soda solution did not decrease the toxicity of the drug, as had been reported by Levaditi (personal communication to Kolle). Whereas one of Collier and Evers' rabbits which had received 0.2 gm. per kilogram of stovarsol suspended in soda solution had survived,

the other 3 which had received 0.1, 0.3, and 0.4 gm. per kilogram, respectively, died. Anderson and Leake found that the rabbits receiving lethal doses lost weight rapidly. Lethargy, anorexia, abdominal distension, and soft stools were noted. Immediately before death the pupils became constricted, respiration was increased, the abdomen became distended, the muscles relaxed, and on stimulation clonic convulsions resulted.

Raiziss, Severac and Moetsch (*166*) carried out experiments with acetarsone which had been prepared in their own laboratory. The maximum tolerated dose (obtained with exceptionally good samples) was 1 gm. per kilogram on peroral administration to the rabbit; the average maximum tolerated dose being 0.8 gm. per kilogram and the lethal dose 1.5 gm. per kilogram. The tolerance of rabbits for this drug, therefore, was 2½ times that determined by the French investigators for stovarsol. In the same experiment, acetarsone obtained on the market proved lethal for rabbits in the dose of 0.5 gm. per kilogram and was tolerated in the dose of 0.4 gm. per kilogram. These authors attributed the lower toxicity of their drug as compared to that determined by all other authors to the greater purity of their own preparation. This presumption appears to have no basis in fact, when the great variability in tolerance for this drug is considered. Very considerable differences can be found in the reports of various authors. This is true even when several authors have used exactly the same preparation of acetarsone. Furthermore, chemical studies of 594 (toxicity as determined by Schlossberger was found to be the same as that of spirocid as determined by Collier and Evers) carried out at the Speyer-Haus showed it to be crystalline and chemically pure.

Kolmer and Rule (*100*) used the same preparation of acetarsone as Raiziss and coworkers. They found that white rats were able to tolerate as much as 10 daily doses of 1.0 gm. per kilogram perorally while rabbits sometimes developed severe diarrhea and died following 3 to 4 daily doses of 0.02 to 0.04 gm. per kilogram. They reported that for the rabbit single doses varying from 0.8 to 1.5 gm. per kilogram produced severe enteritis with death in from 1 to 3 days and represent the minimum lethal dose. The maximum single tolerated dose varied between 0.3 and 0.8 gm. per kilogram. When acetarsone was given daily for 7 days followed by a rest period of 5 days and a repetition of the course, the maximum tolerated dose was from 0.02 to 0.03 gm. per kilogram. A dose of 0.005 gm. per kilogram was given daily to some rabbits for 60 doses without toxic effects.

Baccaredda (*9*) in experiments on 10 rabbits found the minimum lethal dose of stovarsol perorally for rabbits to be about 0.15 gm. per kilogram (0.20 gm. for a rabbit weighing 1,500 to 1,600 gm.), and in experiments on 6 rabbits the minimum lethal dose of sodium stovarsol given by mouth was about the same.

Rosahn and Kemp (*171*) based the dosage in their toxicity experiments on Kolmer's maximum tolerated dose. They began treatment of 12 rabbits with latent syphilis by means of a daily dose of 0.025 gm. per kilogram stovarsol and planned to give this for 7 consecutive days, followed by a rest period of 5 days and a repetition of the course. However, marked loss of weight and diarrhea made it necessary to suspend treatment after the fifth dose. Eleven of the twelve animals died in from 4 to 12 days, the females being apparently somewhat more susceptible to the drug than the males. The author pointed out that the actual daily dose of stovarsol represented only five-sevenths of 0.025 gm. or 0.016 gm. per kilogram because they had found that stovarsol constituted only five-sevenths of the total weight of the preparation used (purchased in the open market). They tried another dosage which had been reported by Kolmer to produce healing and sterilization in syphilitic rabbits, this dose being 0.01 gm. per kilogram 3 times a day for 6 days, followed by a rest period of 5 days and a repetition of this procedure for 8 courses. Six rabbits were treated in this manner, the drug used being acetarsone which was also purchased in the open market. All the animals died after receiving treatment for from 3 to 10 days. Only 1 rabbit survived long enough to receive the second course, but even this animal died before the second course was completed. Another dosage tried was 0.02 gm. per kilogram of acetarsone given daily for 6 days, followed by a rest period of 5 days and a repetition of this procedure for 4 courses. Only 2 out of 6 animals with early syphilis which were treated with this dosage lived long enough to complete the last course. The 4 others died after receiving 3, 5, 5, and 18 treatments. Finally, the dose was decreased to 0.015 gm. per kilogram daily, and 4 courses of 6 daily treatments each with 5-day rest intervals between courses were given. All of 5 rabbits so treated survived the 4 courses. The same procedure was therefore repeated with 24 rabbits, 12 of which had early and 12 late syphilis. The same lot of acetarsone was used. Eight of the animals with early syphilis died after from 5 to 23 treatments, and in 1 of the surviving 4 a metastatic eye lesion developed 42 days after the last treatment. Three of the animals with late syphilis died, and in 2 of the 9 survivors metastatic lesions in the eye developed 25 and 82 days after the last treatment.

Most of the rabbits under treatment presented toxic signs after a few doses. The first sign of toxicity was a listless, sluggish demeanor, accompanied by a dull, vacant stare. The fur became rough and ragged; the animal lost weight and the stools changed from formed to semisolid feces and finally to thin mucous dribbling. Toward the end a severe nasal discharge with crust formation was frequently noted. Animals which were allowed rest periods between courses often recovered rapidly.

Autopsy Findings in Animals Dying From Acetarsone Intoxication

The pathologic findings in the animals examined by Worms (*218*) were extremely variable and in general did not correspond to the size of the dosage administered. In the most marked, but rare, cases petechial hemorrhages of the gastric mucosa as well as of the serosa of a portion of the cecum, edema of the entire intestinal mucosa, hemorrhagic content in the large intestine, ulceration of the mucosa of the large intestine in various places, hyperemic, edematous and slightly enlarged kidneys were found. In the majority of cases the macroscopic findings were limited to the kidneys and cecum, the kidney being most often involved. Histologic findings were few with the exception of hemorrhages of the mucosa of the stomach and intestine. In the kidneys hyperemia, especially of the glomerular capillaries, was observed. However, no extravasates or degenerative processes could be found.

Heitzmann, (*77*) who made histologic examinations of the organs of 3 rabbits and 1 guinea pig out of the series of animals which had been treated by Worms, found the effect of moderately toxic (curative) and lethal doses of the drug to be the same, the only difference being one of degree. Following lethal dosage there was marked destruction of cells in the blood as well as in the excretory organs such as the kidneys. Hemosiderin deposits were seen in the spleen and liver. The kidneys showed epithelial necroses with some evidence of calcification. Following curative dosage there was also hemosiderin deposition in the spleen and liver, but the kidney epithelium showed evidence of regeneration and absorption of calcium deposits. Various organs of all of the animals showed fatty degeneration of the cells. This finding was especially marked in kidneys, liver, heart, and muscles of mastication. The author attributed this change to metabolic disturbance resulting from the toxic action of the drug. He attributed the marked loss of weight, nearly one-tenth of the body weight, to disturbance in body metabolism caused by the toxic action of the drug. Two of the rabbits showed areas of necrosis in the muscles of mastication.

According to Collier and Evers (*36*), autopsy of treated animals revealed lesions in the kidneys and cecum. They found the kidney to be red and edematous, whereas the cecum was edematous and showed the typical picture of arsenic poisoning.

Poole (*164*) performed autopsies on all of his animals which died. In all cases the stomach was found to be enormously distended with food. One animal showed deep jaundice and several exhibited what appeared to be a terminal pulmonary congestion. The intestines were injected in most cases but no hemorrhages were seen. No macroscopic changes in the liver or kidneys were noted. Histologic study of the organs was not made.

The findings of Anderson and Leake (*3*) in animals which had died from lethal doses were distension of the stomach, large intestine, and bladder; congestion of the lungs, liver, and kidneys; and occasional hemorrhages in the kidneys. Microscopic examination revealed congestion of the lungs, liver, spleen, and kidneys with deposition of pigment in these organs. The liver cells were filled with fat globules. Tubular degeneration of the kidneys with occasional hemorrhages was seen in several sections.

Kolmer and Rule (*100*) found no tissue changes of lungs, heart, liver, kidneys, or spleen on histologic examination of rabbits which had received 0.005 gm. per kilogram daily for 56 doses or 0.02 gm. per kilogram daily for 14 doses. But animals which had received 0.04 and 0.06 gm. per kilogram daily for 5 to 7 doses showed varying degrees of fatty degeneration of the liver, cloudy swelling of the tubular epithelium of the kidneys, and acute catarrhal and exfoliative enteritis which was especially marked in the ileum.

The most frequent pathologic findings observed by Rosahn and Kemp (*171*) in their rabbits were edema and hyperemia of the intestine, especially the cecum and ileum; in a few animals there were petechiae on the serosa. The condition of "red kidney," as described by Worms and by Heitzmann was found in some animals whereas in others the kidneys were pale. Histologic examination was not made.

Curative Action of Acetarsone by Mouth in Experimental Syphilis

As already described in detail, the curative action of stovarsol in experimental syphilis was studied by Levaditi and coworkers (*116*) in only 2 rabbits and 1 monkey (the third rabbit in their series had Spirochaeta cuniculi infection). One of these rabbits was cured with 2 doses of 2 gm. each or 1.5 gm. per kilogram and the other with a single dose of 2 gm. or 0.66 gm. per kilogram. The Macacus cynamolgus monkey was cured with 2 doses of stovarsol consisting of 1.5 and 1.0 gm., respectively.

Worms (*218*) studied the therapeutic action of two preparations of acetarsone, namely, the French stovarsol and the German spirocid, in rabbits inoculated with Sp. cuniculi and with 3 strains of treponemes. Three out of 5 animals inoculated with the Reichgesundheitsamt's (R. G. A.) strain were treated with 0.25, 0.33, and 4 x 0.017 gm. per kilogram of stovarsol and 2 of them with 0.25 and 10 x 0.017 gm. per kilogram of spirocid respectively. In 3 of these a cure did not result, recurrences being observed after from 6½ weeks to 3 months and the rabbit which had received 4 x 0.017 gm. per kilogram died on the ninth day. The rabbit which had received 10 x 0.017 gm. was cured; however only after 50 days. Three rabbits were in-

oculated with the Truffi strain. The first received 0.125 gm. per kilogram of stovarsol and 17 days later 0.3 gm. per kilogram. The other 2 rabbits received 0.25 and 0.33 gm. per kilogram of stovarsol, respectively. The first 2 animals were not cured, recurrences being observed after 72 and 85 days respectively, and the third animal died of intercurrent infection on the twentieth day, cure being questionable since the length of the observation period was too short to establish definite cure. Ten rabbits were inoculated with the Nichols strain. Nine of these were then treated with one or the other drug in single dosages varying from 0.125 to 0.33 gm. per kilogram and 1 rabbit with 2 doses of 0.17 gm. per kilogram. Two animals which had received single doses of 0.17 gm. per kilogram were apparently cured, having had no relapse of the infection during an observation period of 3 and 5 months, respectively. Two others, following treatment with 0.23 and 0.33 gm. per kilogram, died on the fourth and ninth days with no evidence of resolution of the lesions. The remaining 6 died, 11, 12, 16, 17, 18, and 45 days after treatment at which time they were apparently cured. But here again the observation period was too short to establish cure. Lymph-node or organ transfers were not made. Worms pointed out that the rabbits with cuniculi strain infections and with Nichols-virus infection responded better to treatment with this drug than those infected with the Truffi and the R. G. A. strains.

Collier and Evers (*36*) inoculated rabbits intratesticularly with pieces of Truffi chancre. When the syphilitic lesions were well developed stovarsol was given by mouth. Two rabbits, of which one had received a single dose of 0.045 gm. per kilogram and the other 0.06 gm. per kilogram on the first day and 0.03 gm. per kilogram on the second day, showed a slight decrease in the number of spirochetes in the lesions and died on the eighth and sixth days, respectively, without having been healed. Another rabbit which had received a single dose of 0.09 gm. per kilogram survived but was not cured. One rabbit received on the first day 0.025 gm. per kilogram without any effect on the chancre and on the fourth day 0.125 gm. per kilogram which resulted in disappearance of spirochetes on the sixth day and in typical healing of the chancre on the forty-fifth day. This animal was observed for 4 months and remained free from recurrence. Four other rabbits which received still higher doses, 0.18, 0.19, 0.25, and 0.28 gm. per kilogram, had negative spirochete findings on the fourth day after treatment; 3 remained alive and were clinically cured 44 and 45 days later; 1 rabbit which had received a dose of 0.19 gm. per kilogram died on the twelfth day. These results showed that stovarsol given orally can cure syphilitically infected rabbits only in a minimum dose of 0.15 gm. per kilogram; this dosage was considerably above the well-tolerated dose. A well-tolerated dose was found to be too small to result in cure. Collier and Evers also pointed out that the disappearance of spirochetes

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from the lesions following stovarsol therapy is much slower than following arsphenamine therapy.

Poole (*164*) treated 6 rabbits having syphilitic orchitis with a single dose of 0.5 gm. per kilogram stovarsol (original French preparation) by mouth. All of them died in from 16 to 27 days after treatment. The duration of the orchitis after treatment was from 11 to 20 days. Lymph-node and organ transfers from 3 of these rabbits to normal animals gave negative results.

Raiziss and Severac (*167*) tested the curative action of acetarsone which had been prepared in their own laboratory on only 1 rabbit, using peroral administration. This rabbit which had well-developed syphilitic lesions was given 6 doses of 0.05 gm. per kilogram each over a period of 11 days. Treatment was then interrupted because the animal was losing weight, but was resumed 32 days later at which time 4 weekly doses of 0.05 gm. per kilogram were given. No relapse occurred during 167 days of observation. Lymph-node transfers made at this time were negative. The authors concluded that the treatment consisting of 10 repeated doses of 0.05 gm. per kilogram of stovarsol was effective.

Kolmer and Rule (*100*), using the Raiziss preparation of acetarsone, tested its curative effect when administered by mouth in varying dosage on a total of 19 rabbits with experimental syphilis. Each of four rabbits received a single dose of 0.5 gm. per kilogram. This resulted in gradual healing of the lesions with negative lymph-node transfers. Each of 2 rabbits received a single dose of 0.2 gm. per kilogram. The testicular lesions healed but the lymph-node transfers were positive. Each of 3 rabbits received a single dose of 0.1 gm. per kilogram. In these, healing of the lesions also occurred but the lymph-node transfers were again positive. The authors concluded that a single curative dose is more than 0.2 gm. and probably less than 0.5 gm. per kilogram. A dosage of 0.005 gm. per kilogram 3 times a day for 1 week followed by a rest period of 5 days and a repetition of the course for a total of 8 courses was given to 6 rabbits. This resulted in gradual healing of the lesions, associated with marked loss of weight of the animals, but all the lymph-node transfers were positive. Four other rabbits were treated in the same manner but with a dosage of 0.01 gm. per kilogram 3 times a day. There was complete healing of the lesions and the lymph-node transfers made after the 8 courses of treatment were all negative.

Rosahn and Kemp (*171*) gave stovarsol by mouth to 2 groups of syphilitic rabbits. The first group consisted of 12 rabbits with early syphilis and the second group of 12 rabbits with late syphilis. In spite of the fact that toxicity experiments had shown that all 5 animals treated with daily amounts of 0.015 gm. per kilogram for 4 courses of 6 treatments each, with 5-day rest periods between courses survived, the same dosage and

method of administration resulted in the death of 8 out of 12 early syphilitic rabbits and of the 3 of those with late syphilis. Therefore a total of 11 (45.8 percent) of the treated animals died. Death occurred after from 5 to 23 treatments. One of the 4 surviving early syphilitic rabbits developed a metastatic eye lesion 42 days after the last treatment and 2 of the 9 survivors in the late syphilitic group developed typical metastatic eye lesions 25 and 82 days after treatment was stopped. Because of the high proportion of generalized lesions (23.1 percent) lymph-node transfers from the remaining survivors were not made.

Prophylactic Action of Acetarsone by Mouth in Experimental Syphilis

As already described in detail, Levaditi and coworkers (*116*, *117*) found stovarsol administered perorally 2 hours to 7 days after experimental syphilis infection to be prophylactically effective. As determined on a series of 21 rabbits, all but 1 of which received single doses, the minimum effective dose was a single dose of 0.1 gm. per kilogram (2 rabbits). The rabbits were observed for from 24 to 76 days, and only 1 of them developed lesions. However, these lesions did not appear until 75 days after treatment. Possibly more of the rabbits might have been found to develop lesions had they been observed over a longer period of time. Lymph-node or organs transfers were not made. Therefore the possibility of latent infection was not eliminated.

Worms (*218*) administered stovarsol and spirocid prophylactically to 16 rabbits 2 hours after scrotal inoculation with the Nichols strain of T. pallidum. Of 4 rabbits which received stovarsol (0.25 gm. per kilogram) 2 died 8 and 16 days later, 1 died of an intercurrent infection, and the fourth did not develop syphilitic manifestations during a 4-month observation period. Of 4 rabbits which were treated with 0.25 gm. per kilogram of spirocid, 3 died 8, 8, and 10 days later, while 1 did not develop manifestations during a 4-month observation period. One rabbit was treated with 0.1 gm. per kilogram of stovarsol and another with the same dose of spirocid; one of these died 6 and the other 7 days after treatment. A chancre developed in 1 rabbit 23 days after it had received 0.033 gm. per kilogram of spirocid and in another rabbit 36 days after it had received 0.033 gm. per kilogram of stovarsol. One rabbit received 0.033 gm. per kilogram of stovarsol 6 days before and again 2 days after inoculation; a chancre developed 51 days later. Another rabbit was treated with 0.033 gm. per kilogram of spirocid on the day of inoculation and again 2 days later; a chancre developed 46 days later. Each of 2 rabbits was given 4 doses of 0.017 gm. per kilogram each administered on the day of the inoculation

and 4 days later (1 received stovarsol, the other spirocid). In the one treated with stovarsol a chancre developed after 46 days whereas in the one treated with the same dose of spirocid syphilis did not develop during a 4-month observation period.

Worms chose the dosages of 0.017 and 0.033 gm. per kilogram in his prophylactic experiments on rabbits because they were comparable to maximal doses for man of 1 to 2 gm. per day. He wanted to determine whether these amounts, given at intervals of 1 to 2 days as the drug is administered prophylactically in human syphilis, would have a prophylactic effect in these animals. His findings are important because they indicate that the dosage corresponding to that used in man is not sufficient to produce a definite prophylactic effect against the infection. Worms concluded that the numerous failures with therapeutic high dosage as well as with prophylactic small and large doses throw great doubt on the dependability of this drug.

Collier and Evers (*36*) gave stovarsol by mouth to 10 rabbits 1 day after inoculating them intrascrotally with the Truffi strain. All 5 animals which had received a dose of 0.2 gm. per kilogram died in from 6 to 26 days (coccidial infection suspected in 1), and in 1 bilateral chancres developed after 46 days. In a series of 4 rabbits which had received 0.1 gm. per kilogram of stovarsol 2 hours after infection, 1 died 9 days later and in 3 chancres developed. The authors then decided to determine the effect of repeated small doses. Three rabbits received 0.075 gm. per kilogram on the first and again on the fourth day after infection; they all died in from 10 to 16 days. Of 3 rabbits which had received 0.05 gm. per kilogram 1 and again 3 days after infection 2 died in from 9 to 18 days and in 1 a chancre developed 160 days after inoculation. To 8 rabbits doses of 0.025 gm. per kilogram were given 1 hour, 1 day, and 2 days after inoculation; 6 of these died in from 4 to 15 days and in the 2 surviving rabbits no infection developed. These results showed that stovarsol even in toxic doses does not have a definite prophylactic effect in experimental rabbit syphilis.

Efron and Lipskerov (*51*) inoculated rabbits intrascrotally with syphilitic virus (strain not indicated). To 3 rabbits they gave by mouth a single dose of 0.16 gm. per kilogram of sodium stovarsol (Russian preparation) one-half hour, 1 hour, and 2 hours after inoculation. To 1 rabbit they gave 0.18 gm. per kilogram 1 hour and 24 hours after inoculation and to 1 rabbit 0.18 gm. per kilogram 2 hours after inoculation. Another rabbit was treated but the dosage which is reported in terms of a 5-percent solution of the drug could not be definitely determined because the weight of the animal was not stated. This animal died 15 days later of pleuritis. The authors stated that negative results were obtained in the 5 rabbits treated, although they did not give the period of observation for all of

the rabbits. The rabbit which had received 0.16 gm. per kilogram in a single dose one-half hour before inoculation and another rabbit which had received 0.18 gm. per kilogram 1 hour and again 24 hours after inoculation were reinoculated 55 days later. Chancres containing spirochetes developed in both after 55 and 26 days respectively. Organ transfers, using the brain and cord, were made from the rabbit which had received 0.16 gm. per kilogram 1 hour before inoculation and had been observed for 103 days and from the rabbit which had received 0.18 gm. per kilogram 2 hours after inoculation and had been observed for 55 days. Of the 5 control rabbits which had been inoculated, 3 gave positive results, 1 remained negative, and 1 died in 3 weeks from diarrhea.

Takatsu (*202*) tested the prophylactic action of a Japanese preparation of spirocid on 7 rabbits which had been inoculated intrascrotally with emulsion of rabbit syphilitic testis. All of them received 0.05 to 0.1 gm. of spirocid per kilogram immediately after inoculation, the same dose being repeated on the following 2 days so that a total dosage of from 0.2 to 0.3 gm. per kilogram was given. Four of these rabbits died on the eleventh to the twenty-third day after inoculation at which time manifestations of syphilis had not developed. Necropsy suggested that death was due to drug intoxication. Three rabbits survived; manifestations of syphilis did not develop during 100 days of observation. At this time they were reinoculated and chancres developed 18 days after inoculation. Lymph-node and scrotal-tissue transfers from the surviving rabbits had given negative results.

Fischl (*59*) reported that he administered to 4 rabbits 2 gm. per kilogram of spirocid in 4 equal doses over a period of 48 hours. Twelve hours later he inoculated the treated rabbits as well as 2 control rabbits with the Truffi strain. In the control rabbits typical chancres developed after a period of 4 weeks whereas the treated animals remained negative during a 6 months observation period. Lymph-node or organ transfers were not made.

Poole (*164*) gave 0.5 gm. per kilogram of stovarsol (Fourneau's original preparation) to each of 6 rabbits 2 hours after inoculation with the Nichols strain. Four of the rabbits died 21, 21, 51, and 66 days later, the last one under ether anesthesia. The 2 surviving rabbits were reinoculated on the seventy-eighth day and clinical signs of orchitis developed in 20 days. Rabits inoculated with the lymph nodes and testes of the 4 prophylactically treated rabbits which died did not give any indication of syphilitic infection.

Raiziss and Severac (*167*) inoculated 10 rabbits with the Nichols strain. In 3 of the animals which were used as controls, syphilitic lesions developed in from 21 to 35 days. The other 7 rabbits received 0.05 gm. per kilogram of acetarsone immediately after inoculation. None of them developed clinical manifestations of infection during an observation period of from

98 to 119 days. Popliteal lymph-node transfers from 6 of these gave negative results. Three other rabbits received 0.025 gm. per kilogram of acetarsone and 1 rabbit 0.01 gm. per kilogram immediately after inoculation. In the last a syphilitic lesion developed on the thirty-seventh day. One of the three which had received 0.025 gm. per kilogram also developed a chancre on the fiftieth day; the other 2 developed no manifestations but their observation period had not been completed at the time this report was made.

Levaditi, Mezger and Schoen (*115*) decided in 1932 to repeat the earlier prophylactic experiments of Levaditi and coworkers. They inoculated 27 rabbits intrascrotally with grafts of Truffi chancre and administered the sodium salt of stovarsol by mouth 20 minutes, 3 days, 6 days, and 7 days afterward. Seven of the rabbits received 0.2 gm. per kilogram 20 minutes, 3 days, and 4 days after inoculation. Six survived and in none of them did chancres develop, whereas chancres were observed in all of 5 control rabbits. Eighteen out of a group of 20 rabbits which had received 0.15 gm. per kilogram 20 minutes, 3 days, 6 days, and 7 days after inoculation "survived beyond the twenty-fifth day." In 2 of these, chancres developed (observation period 30 and 34 days), whereas the other 16 remained negative. The 2 rabbits in which prophylaxis failed had been treated on the third and seventh day, respectively. The lymph nodes of 3 of the rabbits which had received 0.2 gm. per kilogram were examined 33, 41, and 152 days after inoculation, and those of 12 of the rabbits which had received 0.15 gm. per kilogram were examined 37 (two), 41 (three), 42 (four), 51 (three), and 82 (two) days after inoculation, the lymph nodes of two of these rabbits having been examined both 42 and 82 days after inoculation. The results were negative, and reinoculation of these nodes into normal rabbits also gave negative results. Apparently 6 rabbits in this group died before lymph-node transfers were made, but no reference whatever is made to deaths among the animals. This is surprising in view of the fact that it was considered an important factor by other authors.

Kolmer and Rule (*100*) tested the prophylactic effect of acetarsone, prepared in Raiziss' laboratory, on rabbits which had been inoculated with the Nichols-Hough strain. The drug was given 2 hours after inoculation. To 4 rabbits a single dose of 0.5 gm. per kilogram was given. They remained negative, and lymph-node transfers made 5 weeks later gave negative results. Although these rabbits survived they became greatly emaciated. Four control rabbits developed the infection. To 3 additional rabbits single doses of 0.25 gm. per kilogram were given, and the results were the same. Of 4 rabbits which received a single dose of 0.1 gm. per kilogram, 3 remained negative over a period of 4 weeks, and their lymph-node transfers were also negative. The fourth rabbit did not develop

orchitis but its lymph-node transfer was positive. With multiple doses it was found that 0.01 gm. per kilogram 3 times a day for 1 week prevented the development of orchitis and gave negative lymph-node transfers. The number of rabbits which received this dosage is not given. In all of 5 rabbits which received a dose of 0.005 gm. per kilogram 3 times a day for 1 week followed by a 5-day rest period and a repetition of this procedure for 8 courses orchitis developed and lymph-node transfers were positive. On the basis of these findings the authors concluded that the minimum prophylactic dose for rabbits is 0.15 gm. per kilogram in a single dose or 0.010 gm. per kilogram given 3 times a day for at least 1 week. This dosage for the rabbit, they pointed out, would correspond to about 8 tablets of 0.25 gm. each per day for a week for an adult human being (toxic human dose).

In summarizing the results of the French investigators and those of later experimental studies carried out with stovarsol, it will be recalled that Levaditi and coworkers, on the basis of their clinical study of 80 patients with manifestations of syphilis, pointed out that the effect of stovarsol is uncertain. They noted clinical recurrences in 12 (15 percent) of these patients 1 week to 2 months after treatment. Serologic reversal occurred in only 10 patients (12.5 percent). They concluded that the deep action of stovarsol is more variable and uncertain than that of other arsenicals and suggested that the dosage might have to be increased. Because of the uncertain effect they advised that stovarsol be given together with bismuth treatment.

Workers in the experimental field, particularly Worms, Kolle, Collier and Evers, and Rosahn and Kemp showed that stovarsol is much more toxic than was indicated by the small number of experiments carried out by French investigators. Doses comparable to the therapeutic human doses were found to be toxic for animals. Because of great individual variations in the susceptibility of rabbits it was found to be impossible to determine with certainty the nontoxic active dose. A well-tolerated dose was too small to bring about cure, and the effect on the lesions was slower than that of arsphenamine. Doses corresponding to the prophylactic and therapeutic doses used in human syphilis were found to be ineffective in the prophylaxis and cure of rabbit syphilis. The prophylactic and curative effect in experimental rabbit syphilis was not certain even when toxic doses were used.

ACETARSONE IN THE TREATMENT OF ACQUIRED SYPHILIS

Therapeutic Effect

Fourneau's resynthesis of acetarsone, followed by the favorable early reports by Levaditi and coworkers on its antisyphilitic action in experi-

mental as well as human syphilis, led many workers to study its antisyphilitic action in patients with early acquired syphilis in whom the effect of the drug on the manifestations could be observed and compared to that produced by the arsphenamines. At first it was administered intravenously, subcutaneously, and intramuscularly. Laurent (*110*) found that following intravenous injection of acetarsone all of the arsenic introduced into the body in this way was excreted in the urine in 24 hours; following subcutaneous injection its elimination was completed in 3 days. These findings would make subcutaneous injection every 3 days advisable, but it was found impracticable to give injections more than once weekly. Acetarsone administered by these routes, however, was found to have much less effect on the early manifestations of syphilis and on the Wassermann reaction than the arsphenamines—Fournier, Guénot and Schwartz (*63*); Laurent (*110*); Sezary and Pomaret (*187*)—and when administered by the injection method possessed no advantage of any sort over the arsphenamines to justify its use. Levaditi (*114*), who had been studying the peroral administration of bismuth with little success, then decided to observe the effect of acetarsone administered by this route. The studies made by him and his coworkers showed that acetarsone is absorbed rapidly and in considerable quantity from the digestive tract, as determined by the elimination of arsenic in the urine. Clinical observations and animal experiments, particularly the toxicity experiments of Kolle who studied the comparative toxicity by various modes of administration, gave support to the finding that acetarsone is more effective as well as more toxic when administered perorally. The peroral method also apparently has the advantage that by giving divided daily doses the body can be kept more or less continuously under the influence of the drug for a desired period of time without inconvenience. The other methods of administering acetarsone were therefore dropped. When the administration of acetarsone is hereafter discussed it is to be understood that the peroral method was used.

Weitgasser (*212*) administered stovarsol to 4 patients with primary and 2 patients with secondary syphilis. The spirochetes disappeared from the lesions in from 1 to 3 days. The healed primary lesions of 2 patients who had each received 16 gm. of acetarsone were excised and stained according to the method of Levaditi. In spite of the fact that these lesions had healed. spirochetes were still present. Before treatment was given the Wassermann reaction of the blood of 2 patients was negative, but it became positive in spite of treatment; in the other 4 the reaction was positive before treatment and remained so. The patients were observed for from 3 weeks to 2 months, most of them for 1 month.

Gruss (*74*) treated a patient with primary, dark-field positive, seronegative syphilis with stovarsol. From January 10 to February 1 the

patient took 4 tablets every second day. The local lesion was treated with phenol and iodoform because of a suspected mixed infection. On January 27 the lesion was pinhead sized, and the Wassermann reaction was negative. The patient was discharged from the clinic and continued to take 8 more tablets (4 every second day), having received altogether 14 gm. of the drug. On March 1 he returned with a secondary eruption. At this time the primary lesion was still dark-field positive.

Krösl (*104*) used spirocid alone in the treatment of 7 patients with primary seronegative syphilis. The dosage advocated by Levaditi was used, namely, 4 tablets (0.25 gm. each) every second day, the patient receiving 14 gm. in 28 days. Six of the cases remained clinically and serologically negative over an observation period of more than 7 months; the other patient developed secondaries 1 month after treatment was stopped, and these manifestations proved to be very resistant to treatment. In 3 cases of seropositive primary syphilis the blood Wassermann reaction remained positive in spite of spirozid treatment, but a secondary eruption did not appear. Because of the good results obtained in primary seronegative syphilis, Krösl administered spirozid alone to 16 patients with secondary syphilis. Not a single patient became seronegative as result of treatment. The papular lesions were most easily affected by treatment, but the mucosal lesions responded less well. The results of spirozid alone in the late manifestations of syphilis and in cardiovascular syphilis were found to be decidedly inferior to those obtained with neoarsphenamine. Because of this poor therapeutic effect of spirozid alone, Krösl (*103*, *105*) gave intravenous northovan in addition to spirozid to the majority of the series of 73 patients in all stages of syphilis which he reported.

Spiethoff (*195*) treated 2 cases of primary and 5 cases of secondary syphilis by means of stovarsol alone. The course of treatment averaged 5 months, being somewhat longer for some patients and somewhat shorter in primary syphilis. The dosage consisted of 4 tablets a day (the whole daily dosage being administered 1 hour before breakfast) for 7 days, followed by a rest period of 7 days. The drug failed in 1 case of primary and 1 case of secondary syphilis. In the others the effect on the manifestations as well as on the Wassermann reaction corresponded in general to that obtained with arsphenamine. The influence on the spirochetes was, however, less marked.

Lehner and Radnai (*111*) used stovarsol exclusively in the treatment of 3 cases each of seronegative primary syphilis and secondary syphilis. The dosage given was 1.0 gm. in the morning before breakfast for 4 days followed by a rest period of 3 days. All three of the primary cases received a total of 4.0 gm. of stovarsol. The dark-field was still positive 8, 4, and 4 days after treatment was started. In the first 2 cases the lesion epithelized.

The Wassermann reaction became positive in the first case but remained negative in the other two. After 4 gm. had been given, treatment was continued with neoarsphenamine and bismuth. The three patients with secondary syphilis received 16, 16, and 8 gm. of stovarsol, respectively. Some secondary lesions were still present after this amount of drug had been given, and the Wassermann reaction was strongly positive. These authors advised against the use of stovarsol in primary seronegative syphilis and stated that its use is indicated only in exceptional cases in which it is impossible for the patient to get arsphenamine, as for example on trips to remote places, in which case it could be combined with mercury rubs.

Bruhns and Picard (*23*, *24*) treated 53 cases, 48 receiving spirocid and 5 stovarsol, followed by bismuth therapy. In a few cases bismuth was given concomitantly. Two types of dosage were used. Either 2 tablets on the first day and 3 tablets on each of the second and third days followed by a rest period of 3 days and the administration of 4 tablets in 3 days and another rest period or, 4 tablets every 2 days. The entire daily dose was given one-half hour before breakfast. The total dose was 14 gm. Most of the patients had early secondary syphilis, a few had late secondary or tertiary syphilis. Spirochetes disappeared from the secretion obtained from secondary papules after an average dose of 11 tablets. Among 27 cases of early secondary syphilis the Wassermann reaction reversed to negative in 6 cases at the end of the course of spirocid alone, less positive reactions were obtained in 9 and the reaction remained strongly positive in 12 cases. Papular skin lesions healed in from 2 to 4 weeks. Roseola and mucous membrane lesions responded more promptly. In 1 case of hypertrophic papules there was so little effect after 34 tablets of stovarsol that bismuth and neoarsphenamine were started. In a second case of failure the drug was stopped after 37 tablets, and in a third case of failure hypertrophic papules were present after 56 tablets had been given. In this case the Wassermann reaction was strongly positive. These authors concluded that although spirocid is effective it is not as good as arsphenamine.

Altmann and Eliassow (*2*) treated 15 patients, all but 2 of whom had secondary syphilis, by means of spirozid. They gave 1 to 2 tablets daily and later increased this to a maximum of 3 tablets daily which dosage was given for 3 to 6 days, followed by a rest period of equal length. At first the drug was given after meals, later, on an empty stomach. The total dose was 16 gm. In most cases the spirochetes disappeared from the lesions after 1 to 2 gm. of spirozid, and skin manifestations healed after 1 to 5 gm. Toxic reactions occurred in 7 of the 15 cases and were so severe that treatment could be continued in only 8 patients. These authors advised that spirozid should be given only when the patient can be observed daily.

Luerssen (*119*) treated 7 seronegative and 5 seropositive cases of primary syphilis, 10 cases of secondary syphilis, and 2 cases of seropositive tertiary

syphilis with spirozid. According to the method of Levaditi, he gave on 3 successive days 3 to 4 tablets dissolved in water in the morning one-half hour before breakfast followed by 3 days of rest and then another similar course. In part of the cases treatment was then continued with neoarsphenamine and bismuth, or bismuth alone, in the others with courses of spirozid combined with intramuscular bismuth injections. He found that the effect on clinical symptoms was considerably more rapid than after mercury and often almost as fast as with arsphenamine but that there were frequent failures. Epithelization of moist papules and plaques was observed as early as 4 or 5 days. Some papular eruptions persisted for as long as 30 days. The 2 tertiary manifestations also reacted promptly. In 1 case, however, after rapid superficial healing there was a recurrence of the gummatous lesion after 4 weeks. The effect of stovarsol on syphilitic lesions was carefully studied in 13 patients at 2-hour intervals after the drug had been given. From 50 to 100 microscopic fields were examined for each patient. After the first 2 to 4 hours an increase in the number of spirochetes was usually observed, but after another 6 to 8 hours the number and motility of the spirochetes decreased. In about half of the cases the spirochetes disappeared inside of 24 hours and after 1 gm. of stovarsol; in 5 cases after 48 hours and 2 gm. of stovarsol. In the other 5 cases a total of 3 gm. was required in a period of 3 to 4 days. Only in 2 patients with seronegative syphilis did the spirochetes persist for a period of 14 days. They disappeared rapidly on arsphenamine therapy, showing that they were not arsenic-fast strains. In 1 patient removal of the epithelium of a healed primary lesion and study of the serum obtained in this area showed the presence of spirochetes. In regard to the effect of stovarsol on the Wassermann reaction, it was observed that among 7 cases of seronegative primary syphilis 5 remained permanently negative, and 2 became seropositive after 7 days of stovarsol treatment (later becoming negative on combined stovarsol and bismuth therapy); the positive reactions of 17 patients with primary, secondary, and tertiary syphilis were not influenced by stovarsol. The author stated that this is of no particular importance since the time of observation was short. The results with combined stovarsol-bismuth therapy corresponded to those obtained with combined arsphenamine-bismuth therapy. On the basis of his findings, Luerssen concluded that although stovarsol is an effective antisyphilitic drug it is not nearly so effective as arsphenamine and that it is by no means free from toxic effects. He pointed out that with peroral administration it is difficult to know how much is absorbed by the body.

Mierzecki (*134*) treated 60 syphilitic patients with stovarsol including 1 with seronegative primary syphilis, 5 with seropositive primary syphilis, 43 with secondary syphilis, and 11 with tertiary syphilis. The patients received on the first day 2 tablets, on the second and third days each 3 tablets, then a 3-day rest period, following which the scheme was repeated.

As a rule they received a total dosage of 56 tablets (14 gm.) but several of them received as much as 109 tablets (27.25 gm.) of stovarsol. In the seronegative primary case the spirochetes disappeared in 24 hours, and the serologic reactions, which were observed for 6 months, remained negative. The primary lesion itself healed in 2 weeks. The patients with seropositive primary syphilis received from 9 to 14 gm. of stovarsol. In them spirochetes disappeared from the lesions in 27 hours, and the lesions healed in 2 weeks with the exception of a primary lesion of the lip which persisted for 6 weeks and later healed with local mercury therapy. Reversal of the Wassermann reaction occurred in 3 cases in from 3 to 4 weeks. In 1 of these cases it again reversed to positive after 1 week and did not change on further treatment. In the cases of secondary syphilis the spirochetes disappeared in 24 to 192 hours, and the manifestations disappeared in from 3 to 9 days. In 6 cases however the lesions persisted after the entire amount of treatment had been given (as much as 13 to 25 gm. stovarsol), but all of these disappeared with mercury treatment. The Wassermann reaction was reversed in 18 of these cases. Only 5 of these cases were kept under observation for 1 year; in all of these the Wassermann reaction was negative at the end of this time. Spinal fluid examinations made in 2 of the patients with secondary syphilis were negative. In the group of tertiary syphilis the average total dose was 27.25 gm. of stovarsol. Gummas responded only slowly to stovarsol in from 3 to 11 weeks and 3 cases of gumma did not heal with stovarsol. The Wassermann reaction in this group of tertiary syphilis did not reverse. These results led Mierzecki to conclude that although stovarsol cannot be said to have no antisyphilitic properties, it must be considered to be far inferior to neoarsphenamine.

Bruck (*22*) treated 2 cases of seronegative primary syphilis and 19 cases of secondary syphilis with spirozid. The drug was administered every second day for a period of 17 days, the daily dose being 2 tablets for each of the first 2 days of treatment, 3 tablets for each of the next 2 days of treatment and 4 tablets on each treatment day thereafter. Following 1 week's rest a second course was given in the same manner over a period of 15 days, the dose being 4 gm. per treatment day with the exception of the first day on which only 2 gm. were given. A rest period of 2 weeks followed the second course. Altogether 5 courses were included in the treatment scheme; the third and fourth courses being separated by a 3-week rest period and the fourth and fifth courses by a 4-week rest period. The effect on clinical manifestations was found to be definitely slower than that obtained with combined arsphenamine-bismuth therapy. Primary and secondary lesions usually disappeared during the first 2 treatment weeks but occasionally 3 courses were necessary to produce this result. Each of the 2 patients with seronegative primary syphilis received 4 courses, or 120 tablets. Blood tests were made every month and these were found to remain negative for 4

and 6 months, respectively, after treatment had been stopped; in other words, altogether 8 to 9 months since infection. In secondary syphilis it was found that after 4 courses of spirozid (120 tablets) and a treatment period of about 3½ months, a negative reaction could be obtained in the majority of cases. Of the 19 treated 16 became negative, 2 remained slightly positive, and 1 became less positive than before. The author, however, warned against considering these as definite cures.

Kumer (*108*) treated 10 patients with seronegative primary syphilis and 3 patients with seropositive primary syphilis with a total of 16 gm. of stovarsol, used alone. In the seronegative cases the treatment was successful in 3 patients; these were observed for 4, 12, and 54 months, respectively. Recurrence at the site of the primary lesion occurred in 3 other patients after 4, 12, and 30 months, respectively. Three developed secondary lesions after 2, 4, and 7 months, respectively, and a positive serologic reaction occurred in 1 patient after 3 months. Two of the seropositive cases were successfully treated; they were observed for 2 and 48 months, respectively. There was a serologic recurrence in 1 patient after 9 months. The author concluded that stovarsol in a dose of 16 gm. often fails in the treatment of primary syphilis.

Smelov and Kapabekov (*189*) used osarsol alone in the treatment of various stages of syphilis. The initial dosage of 0.25 gm. per day was gradually increased to 1.0 gm. per day. The total daily dosage was given ½ to 1 hour before breakfast, the drug being administered for 5 days. This was followed by a 3-day rest period and the scheme of treatment repeated until a total dosage of 30 to 40 gm. (1 course) of osarsol had been given. Many of the patients received 2 or 3 such courses. In 4 cases of primary syphilis (3 seronegative and 1 seropositive) the spirochetes disappeared from the chancre in from 3 to 6 days and after the administration of from 1.5 to 5 gm. of the drug. Two of the seronegative cases disappeared from observation after 1 course of treatment, and 1 was observed for 2 years; all 3 remained seronegative during their observation periods. The seropositive case showed only a slight reduction in the Wassermann reaction as the result of treatment. Osarsol was also given to 21 cases of early secondary and 16 cases of recurrent secondary syphilis. Lesions disappeared in from 1 to 3 weeks and adenitis in from 1 to 2 months. There was 1 recurrence following osarsol treatment, and this occurred 5 months after treatment had been stopped. The effect on gummas was not particularly good, at least 25 days being required to heal them and gummas in the region of scars responding poorly. Of 3 pregnant women treated, 1 with latent syphilis had a spontaneous abortion at 5 months after having received 33 gm. of osarsol; treatment had been started in the second month. Another woman with early latent syphilis gave birth to a full-term syphilitic child. She had started treatment at 4½ months and had received 28 gm. of osarsol.

The third woman with latent syphilis had received a total of 85 gm. of osarsol, beginning treatment at 4 months. She had an apparently normal child. These authors presented a table showing the effect of treatment on the blood Wassermann reaction of 38 patients with secondary, early and late latent, and tertiary syphilis. Most of these patients had received 2 and a few 3 courses of treatment. In general the effect on Wassermann reversal in these patients was very slight. These authors considered osarsol to have definite antisyphilitic effect but to be inferior to arsphenamine.

Robinson and Robinson, Jr. (*170*) treated 32 patients (6 white and 26 Negroes) with acetarsone—2 had seropositive primary syphilis, 23 had moist secondary lesions on the genitalia, and 7 had latent syphilis. In 15 patients treatment was begun with 1 gm. daily and to 6 of these 1 gm. daily was given for 3 consecutive days; in 2 the dose was increased to 2 gm. on the second day, and in the remaining 7 the treatment was begun with 1 gm. and continued at 1 gm. daily for the entire course of treatment. In 9 patients treatment was begun with 2 gm. per day and kept at this dose for the duration of treatment. Eight patients were started on 3 gm. a day and continued at this dosage for the duration of treatment. Treatment was given once a day for 7 days and was followed by a 7-day rest period. For the purpose of studying spirocheticidal activity of the drug the patients were divided into 5 groups: (1) Three patients with early syphilis who received each 1, 2, and 3 gm. respectively in a single dose. In the patient who had received 1 dose of 1 gm. the spirochetes persisted in the lesion after 24 hours, in the 2 who had received 2 and 3 gm. respectively the organisms dfsappeared in 24 hours. (2) Seven patients with early syphilis who received 1 gm. a day for 3 days and on whom a darkfield examination was made every 24 hours. All of them remained positive for the 3 days of treatment. On the fourth day 2 gm. were given and in each case spirochetes could no longer be demonstrated 24 hours later. (3) Three patients with early syphilis who were hospitalized for the purpose of more frequent darkfield examinations. The daily doses were 2, 3, and 3 gm., respectively. Darkfield examination was made every 3 hours for the first day and every 24 hours thereafter. The first case became darkfield negative in 24 hours. This patient was treated for 3 weeks and received a total of 32 gm. of acetarsone. At the end of this time all lesions had healed, but a severe papulovesicular dermatitis due to the drug had developed and treatment with acetarsone was discontinued. The other 2 patients continued treatment for 4 and 10 months, respectively, receiving a total of 129 gm. and 396 gm. All lesions healed, and the patients became serologically negative (*4*). In 12 patients with early syphilis treatment was begun with 2 gm. a day; this dosage was continued in 7 patients and was increased in 5 patients to 3 gm. a day. Spirochetes disappeared in the lesions of all of these patients in 24 hours. (5) Seven patients with latent syphilis who were treated in

order to determine the effect of this drug on the blood serologic test. These received 0.5 gm. 2 times a day.

In 15 of the patients with genital and cutaneous lesions, beginning involution was noted in 4 days and in the remaining 3 patients in 7 days. Six of these patients were given arsphenamine and bismuth therapy after the spirocheticidal action of acetarsone was noted and before the lesions had completely healed. Only 13 patients continued under treatment until complete involution of lesions resulted; healing occurred in from 11 to 28 days. Lesions healed no more rapidly with 3 gm. a day than with 2 gm. a day. One of these patients was 4 months pregnant when treatment was begun. She had a chancre on the lip and condylomata lata on the vulva. She continued to take acetarsone until term, and gave birth to a full-term, living, seronegative child which remained clinically and serologically negative over an observation period of 7 months. In 6 cases the exact date of disappearance of lesions could not be ascertained; in 2 of these, severe reactions developed and treatment had to be changed; 4 patients lapsed from treatment.

No change in the serologic reactions (Wassermann and Eagle flocculation tests) was noted in 21 of the 25 patients with early syphilis. The 4 in whom the serologic reactions became negative had received 54 and 108 gm. of acetarsone, respectively. There was no change in the serologic reactions of the 7 patients with latent syphilis. Because many toxic reactions were observed (to be discussed later), the authors decided that acetarsone is a dangerous drug and is contraindicated in the treatment of syphilis.

Oppenheim (*148*, *149*, *150*, *151*, *152*, *153*, *154*, *157*, *158*, *159*) reported that he had obtained good results in a total of 200 cases treated by him with a combination of stovarsol and bismuth. He pointed out that, as Levaditi and coworkers had advised, stovarsol should never be used alone. Early in the course of treatment he gave 1 tablet (0.25 gm.) a half hour before breakfast daily for 3 days followed by a 3-day rest period. To patients who could tolerate this amount without untoward effect he gave 2 tablets on the first and 3 tablets each on the second and third days, followed by 3 days of rest and a similar course until 56 tablets (14 gm.) had been given. In 11 cases of primary and secondary syphilis he reported the disappearance of spirochetes from lesions as early as 7 hours after the administration of 0.25 gm. of stovarsol. He observed very little effect of this treatment on the positive Wassermann reaction.

Beutl (*16*) as well as Heymann (*79*) and later Zakon (*225*) published preliminary reports of favorable results of stovarsol treatment in various stages of syphilis. Only Heymann observed any definite effect on the Wassermann reaction, but he gave no details of his findings and he pointed out that the observation period in his cases had been too short to determine if this effect was permanent.

Cregor and Gastineau (*40*) reported "a beneficial effect" of stovarsol treatment in 1 case of primary, 10 of secondary, and 4 of tertiary syphilis. Scherber's (*176*) results are impossible to evaluate because he alternated courses of neoarsphenamine and bismuth with stovarsol therapy.

Yovanovitch (*224*) pointed out that the results obtained with stovarsol were not constant or permanent enough to justify the use of stovarsol as the only form of treatment of syphilis.

Noguer Moré (*146*) as well as Nabarro (*141*), Farina (*56*), and also Getman (*70*), on the basis of their experience with stovarsol, considered this drug to have antisyphilitic action but to be inferior to the arsphenamines.

Klaften (*97*) treated 25 pregnant women with spirocid and bismuth, using continuous treatment with a dosage of 15 gm. of spirocid per course. The course was followed by a 4-week rest period. All of those women (number not given) who had received a total of 10 to 15 gm. spirocid gave birth to apparently healthy infants. In 2 cases in which treatment had been insufficient, infants were born prematurely. All of the infants had negative spirochete and Wassermann findings of the cord. The roentgen-ray examination of the bones was positive in 1 of the infants. No definite effect on the blood Wassermann reaction of these women following treatment was observed.

Prophylactic Effect

The successful prophylactic use of stovarsol which was reported by Levaditi and coworkers (*116*, *117*) aroused considerable interest among syphilologists. The possibility of almost immediately killing off the comparatively small number of spirochetes which might be present at a site of infection after suspected exposure to syphilis by simply taking some tablets by mouth appeared to offer great advantages.

Yovanovitch (*224*) in Paris observed 50 nonsyphilitic persons who had had sexual relations with syphilitics having contagious lesions and in whom the administration of stovarsol prevented the development of lesions and of positive serologic reactions for syphilis. He concluded that stovarsol undoubtedly had a prophylactic effect.

Rosentul (*175*) studied the prophylactic action of stovarsolan (Russian preparation) in a woman with leprosy who had allowed herself to be inoculated on both arms with serum obtained from an untreated syphilitic lesion. This serum was rubbed into the scarified areas of both upper arms for 10 minutes and then allowed to dry for 3 hours without bandage. After 3 and 13 hours the patient received 2.0 gm. of stovarsolan, respectively. Her skin, lymph nodes, and serologic tests for syphilis remained negative during 7 months of observation.

De Favento (*57*) reported 2 cases in which stovarsol in a total dosage of 4 gm. was used prophylactically in syphilis and found to be effective after

2 to 3 months of observation. The first case was that of a man with a primary lesion who had intercourse with his wife. She was given at once 2 gm. stovarsol and on the next day again 2 gm. During 3 months of observation no manifestations appeared, and the serologic tests remained negative. The second case was that of a man who had a primary lesion and had had intercourse with a nonsyphilitic woman. One day later, she was given 4 gm. stovarsol and remained well during a 2 months' observation period.

De Favento (*58*) in 1926 reported 8 more cases in which stovarsol had been used prophylactically with success. To each of these patients (6 women and 2 men) he gave on the first day 0.75 gm., on the second and third day each 1 gm., then 3 days' rest and a repetition of the course. Five of these patients were observed for 1 year, and 2 for 6 months. Because of its toxicity, De Favento did not recommend the use of stovarsol for the prophylaxis of syphilis in prostitutes.

Martinotti, in discussing De Favento's results stated that he did not consider stovarsol a definite, reliable prophylactic for syphilis.

Kissmeyer (*94*) reported on the prophylactic use of stovarsol in 2 patients in whom there was a possibility of having contracted syphilis. One of these remained well, but in the other, after the usual incubation period, a typical chancre developed.

Audry (*8*) reported the case of a 30-year-old woman who when first seen had a superficial erosion of the right labial commissure which had been present for 15 days and was associated with gingivitis. Four days later there was slight submaxillary adenitis. Both her and her husband's Wassermann reactions were negative. She was not seen until 2 months later at which time she had a positive Wassermann reaction whereas her husband's reaction was negative. Neoarsphenamine-bismuth therapy was given to the woman. The husband received 3 to 4 tablets daily of stovarsol for a period of 6 days followed a by rest period of 1 week. He received altogether 3 such courses. Two months after the completion of his treatment the husband had a positive Wassermann reaction which was confirmed by a repeated test.

According to the observation of Tzanck and coworkers (*208*) a patient who had received 8.5 gm. of stovarsol within a period of 3 months because of an intestinal disturbance had not been protected against infection with syphilis.

Oppenheim (*158*) advocated prophylactic treatment of syphilis with stovarsol, but only when not more than 4 to 5 days have elapsed since exposure.

At the eighty-eighth meeting of the Association of German Naturalists and Physicians held in Innsbruck in September 1924, at the meeting of the Berlin Society of Dermatologists (*128*) in March 1925 and in many

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reports in the literature of this period (*127*), outstanding German syphilologists, including such names as Jadassohn, E. Hoffmann, Spiethoff, Worms, Gruss, Krösl, Gans, Eliassow, Altmann, Pinkus, Weitgasser, Bruhns, Lesser, Uhlenhuth, v. Zumbusch, Schumacher, Kolle, Beutl, Lehner, voiced the opinion that stovarsol (or spirocid) is definitely inferior to arsphenamine in the prophylactic and curative treatment of syphilis. Because of the dangers involved in its prophylactic use most of them were opposed to it, a few violently so, whereas a few felt that it might be tried in exceptional cases under careful control of a syphilologist.

The findings of Worms in animal experiments are important, since they indicate that the dosage corresponding to that used in the human being is not sufficient to produce a definite prophylactic effect against the infection, especially when a comparatively long interval exists between infection and the administration of stovarsol.

Uhlenhuth in a discussion of Worms' report (*216*) stated that because of the difficulty in giving the proper dosage the danger of inadequate treatment with resulting development of neurosyphilis and other late complications has to be kept in mind when peroral administration of chemotherapeutic substances is made use of in the prophylaxis of syphilis in man. According to him, the use of stovarsol by the French in the prophylaxis of syphilis does not have sufficient basis in animal experiments, as shown by the findings of Worms.

Luerssen also pointed out that with peroral administration it is difficult to know how much is absorbed by the body.

Pinkus, as well as Bruhns and Picard, in a discussion of stovarsol prophylaxis agreed that in those rare cases in which they had previously decided to use arsphenamine prophylaxis, arsphenamine should still be used. In those cases, however, in which they had previously made observation without giving prophylactic treatment, and in which possible infection is suspected, spirocid (stovarsol) might be tried under the careful observation of a physician. They pointed out, however, that the animal experiments on stovarsol prophylaxis are not very encouraging. These indicate that in the human being one should not use too small doses. This in itself would make general use of the drug as a prophylactic after each possible exposure to infection impossible.

Pinkus (*163*) stated that in comparison to arsphenamine, stovarsol is greatly inferior for the treatment of syphilis. Stovarsol is able to kill spirochetes in syphilitic manifestations only slowly, as evidenced by the fact that spirochetes have been demonstrated even in cicatrized primary lesions which have been reopened. He compared the action of stovarsol to that of protiodide tablets. In regard to prophylaxis by means of stovarsol he stated that only further observations, which were carefully controlled,

could determine whether the claims of the French investigators had a sound basis.

According to Jadassohn (*86*) stovarsol might be tried as a prophylactic in women who have been exposed to men with florid syphilis, after an examination of the cervix for the presence of spirochetes has been made. He was in general opposed to the use of spirocid as a prophylactic against syphilis.

v. Zumbusch (*227*) published a letter in 1924, in which he severely criticized a translation of Levaditi's report of 1923 on the use of stovarsol in syphilis, referring to it as a miserable combination of partly known, partly false data and that one is right in doubting that a man of Levaditi's reputation is actually the author. He voiced himself as being especially opposed to the use of stovarsol in the prophylaxis of syphilis, pointing out the great danger to the public which would accept such a drug as a sure preventive of syphilis. He said that the aid of the authorities should be invoked by physicians in order to prevent the health and money of the people from being sacrificed to the commercial gain of the distributors.

Hoffmann (*80*) was of the opinion that stovarsol and spirocid cannot be recommended for therapy and prophylaxis.

Bloch (*19*) (Switzerland) stated in regard to the prophylactic use of stovarsol that one should not promise people something which does not exist. He pointed out the danger of self-administered prophylaxis with this perorally used drug, saying that it should remain in the hands of specialists and that each case in which its use is considered should be carefully weighed.

According to Schumacher (*180*, *181*, *182*) unchanged stovarsol has no action on spirochetes in vitro. That stovarsol undergoes a chemical change in vivo is shown by the definite clinical effect which this drug has on syphilitic manifestations. What this change is, is still unknown. Whether it is changed primarily into p-oxy-m-acetylaminophenylarsinoxide or whether it is quickly changed with complete de-acetylization into the p-oxy-m-aminophenylarsinoxide, is of little importance. If only the first change occurred, the drug would have less therapeutic effect than if the change into the latter compound occurred. Even though the latter compound were formed, in other words, assuming the most favorable possibility, stovarsol still would never be an optimal acting antisyphilitic and prophylactic drug. The therapeutic index of stovarsol is considerably lower than that of arsphenamine, since the p-oxy-m-aminophenylarsinoxide which develops is too much water-soluble and too little lipoprotein-soluble. For this reason the product that is formed enters into chemical reaction with the cells of the body. This increases its toxicity, as compared with arsphenamine, and at the same time lowers its therapeutic index.

He said further that the animal experiments of Worms also show the greater toxicity and poorer therapeutic effect of stovarsol as compared with arsphenamine. He reviewed the experiments of Steinfeld (*197*) who showed that its early administration was not able to prevent involvement of the central nervous system in relapsing fever of the mouse. The criticism that these experiments with relapsing-fever spirochetes are not comparable to experiments with syphilis spirochetes is not valid, Schumacher stated, since in the chemical structure of the relapsing-fever spirochete as well, it is mainly a lipoid-protein combination which is concerned. He pointed out also that one cannot expect as rapid and energetic an effect with stovarsol as with arsphenamine because it is absorbed from the gastrointestinal tract in the form of a sodium salt. Since it is thus absorbed only a part of it can be changed into the active principle which gets into the blood stream, a part being rapidly eliminated. In order to get effective action against the spirochetes, a large amount of the conversion product would have to be present in the blood at one time which would require that large doses be administered. This renders the drug unsuitable for prophylactic use since in people who frequently expose themselves to infection there would be danger of intoxication.

In recent years nothing has appeared in the literature to indicate that these German syphilologists have changed their opinion in regard to stovarsol as expressed by them during this earlier period. Fuhs (*67*) of Vienna, in a recent publication on the modern treatment of syphilis did not even mention acetarsone in the treatment of congenital syphilis. Buschke (*27*) advised against the use of acetarsone in congenital syphilis. In Zieler's (*226*) "Lehrbuch und Atlas der Haut–und Geschlechtskrankheiten" published in 1937 the following is said in regard to it: When the intravenous administration of arsphenamine is impossible, for instance, in severe involvement of the internal organs (heart, blood vessels, liver) or in very old people, spirocid may be used. Its chief advantage is its ease of administration. Although it has a definite effect on syphilitic manifestations, its action is undoubtedly weaker than that of arsphenamine. It therefore cannot be considered as an adequate substitute for the latter in the regular treatment of syphilis. According to the findings in animal experiments, the danger exists that the infection has not been cured but only suppressed (as in the prophylactic use of bismuth).

The present day opinion of French syphilologists in regard to the use of stovarsol does not seem to differ essentially from that of German syphilologists. In the Nouvelle Pratique Dermatologique (*43*), edited by Darier, Sabouraud, Gougerot, Milian, Pautrier, Ravaut, Sézary, and Clément Simon, all that is said about stovarsol in the treatment of syphilis is the following: The arsphenamines are the fundamental treatment of

active syphilis: primary, secondary, visceral syphilis, and syphilis of the central nervous system. They are rarely used alone, being usually given together with bismuth or mercury. The pentavalent arsenicals have been extolled for the prophylaxis of this disease, but there seems to be no evidence of their superior efficacy; they are used especially in the treatment of syphilis of the central nervous system, particularly in general paresis and tabes; their efficacy is not questioned, but certain authors deny the claim that it exceeds that of the arsphenamines.

British opinion in regard to acetarsone has been expressed by Burke and also by Nabarro. Burke (*25*, *26*) stated in 1925 and again in 1929, that stovarsol was—so far as curing established syphilis and rendering a positive blood Wassermann test permanently negative—inferior both to arsphenamine and bismuth, but of greater value than mercury. In 1934 Nabarro (*141*) wrote that the evidence for the therapeutic efficacy of stovarsol in congenital syphilis was not conclusive since the cases treated had not been observed long enough to be certain that clinical and serologic relapse would not occur. In Nabarro's (*142*) latest report (1941) he stated that the dearth of reports on the use of stovarsol in Great Britain is presumably prima facie evidence that the drug has found little favor among British venereologists and pediatricians.

In the United States acetarsone has never been accepted for the treatment of acquired syphilis. While it has been used chiefly by pediatricians, in the treatment of congenital syphilis, it has never been accepted by the Council of Pharmacy and Chemistry of the American Medical Association for the treatment of this disease in any of its forms. The opinion of American syphilologists in regard to its use in congenital syphilis will be discussed later.

Toxic Reactions in Adults Produced by Acetarsone Therapy

As v. Veress (*209*) has pointed out, acetarsone is an active drug, and the nature of its action is often unpredictable. Numerous reports in the literature show that it produces toxic reactions in a large percentage of cases treated. Oppenheim (*157*) pointed out that toxic reactions, when not due to idiosyncrasy, are due to errors in the administration of the drug; for example, no treatment-free intervals, a too large dosage. Analysis of the reports of 37 authors on toxic reactions to acetarsone which occurred in a total of 94 patients shows Oppenheim's assertion to be generally true, with the exception that even on moderate dosage over a short period of time the drug cannot be considered safe. In other words, idiosyncrasy occurs almost too frequently to justify the use of that word. Oppenheim used a comparatively low dosage, his scheme of treatment being essentially that advocated by Levaditi. According to this scheme the daily

dose is 0.25 to 1.0 gm. given for a period of 3 days and followed by a rest period of 3 days. The total dosage is 14 to 16 gm. Among those authors who reported toxic reactions and who used the scheme of treatment recommended by Oppenheim the percentage of reactions is lower in general and the toxic effects produced somewhat less serious than among those who used other treatment schemes with the exception of 1 case reported by Mierzecki in which exfoliative dermatitis developed after a total of 14 gm. Included in the group treated with this low dosage are a total of 337 patients among whom 24 had definite toxic reactions (7 percent); among Luerssen's 24 patients, 4 (16 percent) had moderately severe reactions; among Oppenheim's 200, there were 8 (4 percent); among Bruhns and Picard's 53, there were 8 (15 percent); and among Mierzecki's 60, there were 4 (6.7 percent) of these reactions. Some of Mierzecki's patients received a total dosage of 27 gm.

Practically all authors, regardless of the dosage given, have noted mild reactions to acetarsone in the majority of patients treated, consisting chiefly of a Herxheimer reaction with fever at the end of the first day of treatment. Herxheimer reactions occurred in 15 out of Luerssen's 24 patients and in 15 out of 45 patients treated by Bruck. These reactions are usually transitory and do not prevent the further administration of the drug.

Definite idiosyncrasy was manifested by 7 (7.4 percent) out of the total of 94 patients with reactions (observed by various authors). In two of Lehner and Radnai's (*111*) patients, chills, fever, abdominal pain, and diarrhea occurred 6 to 8 hours after the ingestion of 0.5 gm. of stovarsol; treatment with stovarsol was discontinued. In 1 of Altmann and Eliassow's (*2*) patients, who had a history of arsphenamine dermatitis, exfoliative dermatitis occurred following the taking of 0.25 gm. of stovarsol. Another patient with a history of dermatitis as the result of neoarsphenamine therapy was treated with stovarsol by Cazeneuve (*31*). Following the administration of 0.5 gm. daily for 3 days diarrhea, exfoliative dermatitis, and icterus developed in this patient, and he died 1 month after stovarsol therapy had been started. v. Veress' (*209*) patient had a history of nitritoid reaction to neoarsphenamine. This patient had received 0.25 gm. of spirocid daily for 4 days in the treatment of lupus erythematosus when he had an acute reaction characterized by weakness, vertigo, tachycardia, shortness of breath, fear of impending death, confusion, and cyanosis. He recovered following the administration of artificial respiration and the injection of stimulants. One of Izar's (*85*) patients received 0.25 gm. of stovarsol as treatment for intestinal parasites; abdominal pain and vertigo developed. On the following day he took another tablet (0.25 gm.) and 3 hours later had severe abdominal pains, profuse sweating, diarrhea, vesical and rectal tenesmus, vertigo, and tachycardia. Follow-

ing accidental contamination of the eye with infectious syphilitic material, Schwarz (*183*), a physician, administered stovarsol to himself. He took 0.25 gm. 1 hour after the evening meal. Three hours later he was awakened by severe itching and observed a dense scarlatiniform eruption. He did not attribute this reaction to the drug and on the next day, following a purgative, took 0.75 gm. (in 3 doses). Following this there was an exacerbation of the eruption with accompanying depression, malaise, headache, vertigo, anorexia, and an evening temperature of 38.5° C. On discontinuing the drug for 3 days there was gradual improvement. On the fourth day he took 0.5 gm. and on the fifth day had headache, malaise, confusion, diarrhea, abdominal pain, and a drawing sensation in the region of the kidneys. Several days later he observed pain and swelling of all palpable lymph nodes and petechiae on the upper and lower extremities. He had 10 to 17.5 percent of eosinophils. Following discontinuation of the drug there was rapid improvement. To this list of cases might be added that reported by Semon (*185*) of a woman who was treated with stovarsol for "intractable constipation." Two days after receiving a course of treatment with stovarsol in a total dosage of 1.75 gm. in a period of 7 days she developed a scarlatiniform eruption, petechiae on the fingers, edema of the eyelids, hands and feet, and paresthesias of the extremities. Slow elimination of the arsenic through the feces, in view of the constipation, may have been a factor in the toxic reaction in this case.

Four (4.3 percent) deaths occurred in this total series of 94 cases of reactions observed by various authors. One was that of a patient reported by Cazeneuve, who had a history of arsenic idiosyncrasy, which has already been discussed. Benhamou, Temim and Lofrani's (*13*) patient died after the injection of a total of 63 gm. of stovarsol, given by subcutaneous injection in 3 courses in the treatment of tabes. This patient had complete agranulocytosis. Caroli and Mallarmé's (*29*) patient received a second course of stovarsol 6 months after the first course had been given. Although the single doses were small, the courses lasted 15 days, and the patient continued to take the drug after serious symptoms developed. Before death he had purpura, hemoptysis, ulceronecrotic lesions in the mouth and throat, and complete agranulocytosis. Tchetverikov and Semenov's (*203*) fatal case was that of an 18-year-old woman who was treated with osarsol for intestinal parasites. Following the administration of 1 gm. daily for a period of 4 days toxic symptons developed on the fifth day. These consisted of headache, nausea, fever, vomiting, loss of consciousness, generalized papular eruption, and coma. A diagnosis of arsenic encephalitis was made. She died 27 days after symptoms first appeared. At autopsy petechial hemorrhages of the brain and cord, fatty degeneration of the liver, and acute glomerulonephritis were the principal findings.

In general those authors who used a higher dosage, either in terms of the single dose, the length of the treatment period, the shortness or infrequency of rest periods, or total dosage, also reported a higher percentage of toxic reactions and greater severity of these reactions. A patient reported by Michael (*133*) developed an eruption on hands, face and neck, associated with abdominal cramps and nausea, after taking 22 gm. stovarsol in the treatment of colitis. Treatment was continued, and exfoliative dermatitis developed after she had taken a total of 45 gm. over a period of 2 months (dosage 0.75 gm. daily). Aschner (*7*) reported the case of a 34-year-old woman who because of Vincent's angina received spirocid in very high dosage (2 gm. daily for 4 days, then 1 gm. daily for another 4 days). On the ninth day an exanthem developed. Spirocid was immediately discontinued. Two days later a severe confusional state developed, and in 24 hours she went into deep coma. A diagnosis of spirocid encephalitis was made. Porot and Guillain (*165*) reported 3 patients who because of intestinal parasites received stovarsol. In one of these the drug was given over a long period of time, but in the other two the dosage apparently was not excessive. Two of them developed sensory polyneuritis and one both sensory and motor polyneuritis.

Jausion, Longin and Gauch (*88*) reported the case of a 30-year-old man who was treated with stovarsol for malaria. From April 25 to May 5 he received 0.5 gm. daily. On May 5, after 11 days of treatment and a total dosage of 5.5 gm. a vesicular erythematous plaque appeared on the right forearm and became rapidly generalized and very itchy. The physician did not blame stovarsol and kept the patient on this treatment which the patient continued to take irregularly. Leukodermic areas, surrounded by areas of hyperpigmentation, appeared. In November polyneuritis developed, the feet being chiefly affected. He had sensory disturbances, paralysis, atrophy, areflexia, and reaction of degeneration. He made a complete recovery with the exception of a slight impairment of muscular power in the extensor muscles. Schereschewsky's (*178*) patient took 10 gm. spirocid over a period of 14 days in the prophylactic treatment of syphilis. Already 5 to 6 days after starting this treatment he had malaise, somnolence and apathy, which increased. About 1 week after treatment had been discontinued the symptoms were still present and there was a tremor o the hands. Reiter (*169*) reported the case of a 36-year-old man who was treated with spirocid because of a mouth and throat infection. He received a total of 5.5 gm. in 7 days without a rest period. Severe encephalitis developed, from which he finally recovered. The author pointed out that in this case the toxicity of the drug may have been enhanced due to the fact that the patient had an acute infection, and recalled that Ehrlich warned against giving arsphenamine in the presence of acute infections. Segal (*184*) reported the case of a 64-year-old woman in whom encephalitis

developed following treatment of diarrhea with acetarsone. She had received 4.5 gm. acetarsone in 9 days. On the ninth day fever and a rash developed and were followed 2 days later by coma, convulsions, and opisthotonus. Recovery took place with the exception of persistent severe pain and paresthesia in the arms and right leg. Pain and weakness still persisted in the left arm 1½ years after the ingestion of acetarsone. Haberfeld and Rudolph (*76*) treated an 18-year-old woman with lymphocytic angina with spirocid. She received 4.75 gm., but the dosage and length of treatment period are not stated. In the seventh week of her illness she had complete agranulocytosis. She recovered rapidly on omnadin injections. In order to determine whether spirocid could be blamed in this case, the authors gave her 0.5 gm. of spirocid after she had completely recovered. Several hours later the temperature rose to 39.5° C., the patient felt very ill and had a pulse rate of 140.

Somewhat less severe symptoms reported by authors using comparatively high dosage are generalized dermatitis reported by Kromayer (*106*), Hoffmann (*80*), and Krösl (*103*), and diarrhea with tenesmus reported by Weitgasser (*272*). Bender (*12*) reported toxic reactions which occurred in 6 patients treated for amebiasis with stovarsol with a dosage of 0.5 to 0.75 gm. per day for 8 or 9 days. Symptoms appeared after 4.3 to 6.25 gm. had been given and included coryza, malaise, fever, painful adenitis, morbilliform or scarlatiniform skin eruptions (some with purpuric spots), leukopenia and eosinophilia. In Annesley's (*4*) patient, treated for amebiasis with 6 gm. of stovarsol per course of 12 days, followed by a 10-day rest period, symptoms developed 3 weeks after the second course. He had a papular skin eruption of the face, neck, and extremities, edema of face and neck, purpuric spots on the legs, and a temperature of 104° F. Three patients treated with stovarsol by Gaté, Billa, Rousset and Michel (*68*) for various nonsyphilitic conditions all developed morbilliform or scarlatiniform skin eruptions after 5.75, 4.0, and 6.25 gm. respectively. One of these patients also had diarrhea. The daily dose was usually 0.5 gm. but apparently no rest periods were given.

Monnerot-Dumaine (*135*) gave a total dose of 4.25 gm. stovarsol in 5 days to a patient with dysentery. On the eighth day, fever and on the ninth day a generalized, morbilliform skin eruption developed. Castrillon's (*30*) patient was a 30-year-old woman with lambliasis who received 0.5 gm. of stovarsol per day for 8 days, in addition to injections of sodium cacodylate. On the eighth day intense headache, nausea, and vomiting developed. The urine was scant in quantity and contained albumin, hyaline and cylindric casts, and erythrocytes. A generalized scarlatiniform skin eruption appeared, and the gingivae were congested and bled easily. Following the discontinuation of arsenical treatment, the patient made a rapid and complete recovery. Capurro (*28*) reported the case of a man

treated with stovarsol for Blastocystis hominis infection. He received 7 gm. per course of 8 to 9 days. No rest period was given between the first and second course but there was a 10-day rest period between the second and third course. During the last course his skin was itchy, and several days after the last course a generalized papulopustular skin eruption appeared which cleared up rapidly.

For the purpose of making a rough comparison between the percentage of moderately severe toxic reactions occurring in the group of patients treated by the Oppenheim low dosage scheme and that occurring in a group treated with definitely higher dosage a total of 100 patients reported by 4 different authors are included. Among these 100 patients treated, 27 (29.5 percent) had these moderately severe toxic reactions; they include Altmann and Eliassow's 15 patients with 6 reactions (40 percent—the patient with idiosyncrasy is not included), Kromayer's 8 patients with 2 reactions (25 percent), Bruck's 45 patients with 7 reactions (15.5 percent), and Robinson and Robinson, Jr.'s 32 patients with 12 reactions (37.5 percent). It is apparent that a series of 100 patients is not comparable to one of 337 patients, but allowing for this factor the difference between 29.5 percent of reactions in the former group as compared with 7 percent in the latter is sufficient to indicate that a lower dosage scheme produces fewer toxic reactions than definitely higher dosage. Whether it is therapeutically effective is another question.

Izar's (*85*) scheme of treatment appears to have resulted in an even lower percentage of toxic reactions than that of Oppenheim. He gave 0.25 to 0.50 gm. per day for 10 to 15 days and followed this by a 20-day rest period. The total dosage was 14 gm. He reported only 4 reactions occurring among a total of 200 patients treated (2 percent).

Getman (*70*) treated 139 male patients with stovarsol in a somewhat higher dosage than that of Oppenheim. The number of toxic reactions in his group is fairly high but he listed the incidence of different reactions and did not state how many patients had reactions. Since several different symptoms may have occurred in the same patient, it is impossible to determine the percentage of patients who had reactions in his group.

That stovarsol administered by other routes than perorally produces toxic reactions is shown by the following reports: Nicolas and Rousset (*145*) observed an eruption on the buttocks and thighs in a patient with general paresis who had received 50 injections of the drug. In Kesten's (*92*) 5 patients who received "Powdex-formula 21" (stovarsol) by vaginal insufflations exanthemata developed after 1 to 20 treatments. Worms' (*215*) patient inserted stovarsol tablets over a period of time into the vagina for the treatment of discharge. She had fever, scarlatiniform skin eruption, convulsions, and coma but finally recovered.

The rate of urinary arsenic excretion after peroral acetarsone administration was studied by Chen, Anderson and Leake (*33*) in 2 patients being treated with acetarsone for amebiasis and in 2 normal subjects. One patient received a total of 11 tablets (0.25 gm. each) of acetarsone over a period of 6 days. Of a total of 0.756 gm. of arsenic administered, 29 percent was recovered from the urine in 14 days following the beginning of treatment. In a second patient, who received 14 tablets of acetarsone over a period of 7 days, 17 percent of the 0.952 gm. of arsenic administered was recovered during the 10 days after treatment began. In one normal person receiving 0.5 gm. of acetarsone containing 0.138 gm. of arsenic, 20 percent was recovered in 72 hours after giving the drug, but in a second normal person given the same amount, only 7 percent was found in the urine 24 hours following oral administration.

In order to determine the value of routine qualitative tests for arsenic as evidence of whether the patient was receiving acetarsone, Pillsbury and Perlman (*162*) carried out a large number of tests according to the Gutzeit and Reinsch methods. Occasional positive reactions were obtained, but the procedure proved to be of no clinical value. Negative reactions were reported for most of the patients who were definitely known to be receiving acetarsone. No determinations on specimens of the stool were done.

Klaften (*97*) studied the arsenic content of the placenta of women who had received antisyphilitic treatment during pregnancy. He found that after neoarsphenamine treatment, arsenic could almost regularly be detected in the placenta, but after peroral spirocid treatment it could be found only following a total dosage of 7 or 8 gm. In 1 case arsenic was found in the placenta after the administration of 0.5 gm. spirocid on the day before and 0.5 gm. 5 hours before the birth. However, after greater intervals no arsenic could be found in the placenta. This finding led the author to adopt the continuous method of spirocid therapy in spite of the fact that it is not without danger.

Schnitzer (*179*) made comparative studies of intracutaneous sensitization in guinea pigs, using a number of different arsenicals, including spirocid. He found that sensitization could be regularly obtained with the trivalent arsenicals but not with the pentavalent arsenicals.

CONGENITAL SYPHILIS

An antisyphilitic drug for the treatment of infants and small children which can be administered perorally has certain important advantages over one which can be administered only intravenously or intramuscularly, provided, of course, that it is equally effective and no more toxic. All physicians are not expert enough in the technic of intravenous injection always to be able to introduce the needle into the infant's or small child's

vein. The procedure at best involves cries and struggling on the part of the small child which is distressing to the mother even though she does not witness the treatment. Since most congenitally syphilitic children and their mothers are not highly intelligent, it is difficult for them to realize the importance of treatment and they may become conditioned against the disagreeable treatment. Pain and swelling and occasionally abscess of the tissue may result from intramuscular injection. This may prevent the infant which is beginning to learn to stand and walk from continuing its efforts in this direction. The fact that a child is being treated for syphilis can be concealed from the child himself as well as from others much better with peroral than with injection treatments. But there are also certain definite disadvantages of peroral treatment. Infants often refuse to take either food or drink which has the least unusual taste; regurgitation and vomiting are frequent at this age even in normal infants, making the regular administration of the drug difficult. Because of low intelligence, lack of a sense of responsibility, and the difficulties involved, the mothers may not give the prescribed drug to the child, therefore the physician can never be sure whether the child is receiving the drug or how much he is getting. Since haphazard treatment in syphilis is worse than no treatment, the child's chances to be cured of the infection are permanently lost.

As was to be expected, the earliest reports on the treatment of congenital syphilis with stovarsol came from France. In 1924 Dupérié, Cadenaule and Clarac (*47*) published the results of stovarsol treatment of a 2-month-old congenitally syphilitic infant with rhagades, snuffles, and skin eruption. The dosage was 0.062 gm. 2 times daily for 12 days, followed by a rest period of 3 days. After the infant had received a total of 4.5 gm. of stovarsol, the skin eruption had disappeared, and the coryza and general condition had improved. However, little change could be noted in the size of the enlarged spleen and liver. These authors suggested that stovarsol be used together with other specific therapy, preferably with mercury.

Guillemot (*75*) gave stovarsol in a daily dosage of 0.02–0.07 gm., or a total dosage of 0.62 gm. in 13 days to a 15-day-old infant with anal condylomata and a fissure of the lip. The lesions healed promptly. He mentions that at first he used higher dosage which resulted in digestive disturbances and points out that considerable individual variation in tolerance of the drug occurs. Ribadeau-Dumas, in commenting on this report stated that he and Clément Simon had used stovarsol in the treatment of syphilis in infants and that frequently they had found its action to be incomplete.

Following these early French reports, numerous publications on the use of stovarsol in the treatment of congenital syphilis have appeared in the

literature. These have originated chiefly in Germany, Austria, and the United States; a few have come from other European countries and South America. It is surprising that not a single detailed French report on its use in a series of congenitally syphilitic children has appeared. It seems that the following statement by Blechmann and Bohn (*18*) therefore is correct: "It does not seem that in France stovarsol actually occupies the important place which foreign authors, especially those in the United States, Germany, and Austria, are more and more inclined to assign to it in the treatment of congenital syphilis, especially syphilis of the newborn and the nursling."

Among the various authors who have reported on the treatment of congenital syphilis with acetarsone there has been a great difference of opinion in regard to the dosage and plan of administration of the drug. For convenience the treatment schemes used can be divided into low dosage, high dosage, continuous and intermittent treatment, and the use of acetarsone alone or in combination with either bismuth or mercury or iodides. The more important of these schemes are shown in table 1.

TABLE 1.—*Representative schemes of acetarsone dosage in congenital syphilis*

Author	Plan of treatment	Length of treatment-time	Total dose
	Low dosage-Intermittent scheme		*Gm.*
Oppenheim.....	2–3 days treatment followed by 2–3 days rest. Daily dose: Newborn: 0.01–0.03 gm. Infants up to 6 months: 0.05–0.12 gm. Infants up to 1 year: 0.06–0.20 gm. Children: 0.25–0.5 gm.	3 months...	[1] 1–3
	Low dosage-Continuous scheme		
Bratusch-Marrain ...	1st week—7 days—0.005 gm. per kg. daily. 2d week—7 days—0.010 gm. per kg. daily. 3d week—7 days—0.015 gm. per kg. daily. For next 6 weeks—0.020 gm. per kg. daily. Rest for 4–6 weeks. These courses to be repeated until the Wassermann reaction which is taken after each course is negative 3 times in succession.	9 weeks....	.....

[1] Bismuth also given.

TABLE 1.—*Representative schemes of acetarsone dosage in congenital syphilis*—Con.

Author	Plan of treatment	Length of treatment-time	Total dose
	High dosage-Intermittent scheme		
Müller, E.....	Infants under 2 years of age. Give only 1 course—3 months: 10 days treatment followed by 4 days rest. 1st period 0.25 gm. daily. 2d period 0.25–0.375 gm. daily. 3d period 0.375–0.5 gm. daily. 4th period 0.5–0.75 gm. daily. 5th period 0.75–1.0 gm. daily. 6th period 1.0 gm. daily. 7th period 1.0 gm. daily.	3 months...	40–55
	High dosage-Continuous scheme		
Tuscherer.....	For 3 days 0.062 gm. daily (1 dose)..... For 3 days 0.125 gm. daily (2 doses). For 3 days 0.187 gm. daily (3 doses). For 3 days 0.250 gm. daily (4 doses). For 3 days 0.375 gm. daily (3 doses). For 3 days 0.500 gm. daily (4 doses). For 3 days 0.500 gm. daily (2 doses). For 20 days 0.750 gm. daily (3 doses).	41 days....	21
Maxwell and Glaser .	1st week—0.062 gm. daily (1 dose) ..... 2d week—0.125 gm daily (2 doses). 3d week—0.187 gm. daily (3 doses). 4th week—0.250 gm. daily (4 doses). 5th week—0.375 gm. daily (3 doses). 6th week—0.500 gm. daily (4 doses). 7th week—0.500 gm. daily (2 doses). Then 6 weeks rest period.	49 days....	14

RESULTS OBTAINED WITH LOW DOSAGE-INTERMITTENT SCHEME

Oppenheim and Fessler (*155*) reported on the spirocid treatment of congenital syphilis in 11 infants under 1 year, 15 children from 3 to 13 years of age, and 8 patients whose ages were 16 to 26 years (table 1). In slightly more than half the total number of patients treated spirocid was used alone, in the others it was given together with mercury or bismuth administration. In the former group 22 percent showed "improvement" in the Wassermann reaction as the result of treatment, including 8 percent who had reversals to negative. In 8 percent the reaction increased in intensity and remained unchanged or variable in the others. In the latter group 33 percent showed "improvement" in the Wassermann reaction, including 11 percent of reversals to negative. In 5.6 percent the reaction increased in intensity and remained unchanged in the others.

Oppenheim (*156*) in 1930 reported that he found spirocid of value in the treatment of congenital syphilis involving the skin and mucous membranes, that in the eye manifestations of congenital syphilis the combination spirocid-bismuth was just as effective as arsphenamine but that the serologic reactions were not as quickly influenced as with arsphenamine.

Scherber (*177*) reported on an incomplete study of the drug in a series of 22 children of whom 9 were less than 1 year of age. He gave 5 days of treatment followed by 5 days of rest; the total dosage was 2 to 3 gm. in 10 weeks. Of these 9, definite manifestations of syphilis were noted in 3, whereas in 6 no manifestations were present, and their serologic reactions were negative. Healing of the lesions of interstitial keratitis and improvement in the Wassermann reaction occurred in a 14-year-old girl and an 8-year-old boy after they had received 2 courses, the total dosage being 25 gm. and 15 gm. respectively. Four other children who were still under treatment for interstitial keratitis at the time of Scherber's report had shown some clinical but practically no serologic improvement. In a boy with gummatous periostitis of the knee joint no improvement occurred after he had received 3.75 gm. spirocid.

Vohwinkel (*210*) advocated the use of spirocid in the dosage suggested by Oppenheim as additional treatment for children in the rest periods between arsphenamine-heavy metal courses of antisyphilitic treatment, and as prophylactic treatment of apparently healthy infants whose mothers had received inadequate treatment during pregnancy. In his opinion spirocid was not a sufficiently effective antisyphilitic drug to justify its being used alone. He advised the use of 1 or 2 courses of spirocid in the prophylactic treatment of infants.

Results Obtained With Low Dosage–Continuous Scheme

Juarros and Galarreta (*91*) reported on the results of 3 months of treatment with spirocid of a group of 40 children aged 1 to 16 years, the majority being between 5 and 13 years. The dosage per course was 2 to 7 gm. in 3 months. The serologic reactions showed "improvement" in roughly half of these patients. There was also some improvement in the mental condition of the same number of children.

Danzer (*42*) treated four infants prophylactically on the basis of the finding of a positive Wassermann reaction in the mothers. The dosage per course of 3 months was 3 to 5 gm. They received from 1 to 3 courses of spirocid and remained free from syphilis during an observation period of from 3 months to 2½ years. She also administered spirocid to 16 infants with positive Wassermann reactions. A syphilitic exanthem was present in 10 infants in this group. Four of them died shortly after coming to the hospital (cause of death not given); 4 died later of pneumonia and menin-

gitis. Of the 12 in whom some appraisal of the treatment could be made, 6 became seronegative after 1 to 3 courses; in 3 the serologic reaction remained strongly positive, and in 3 the reaction became negative and later strongly positive again. The length of the observation period for this group is not given.

Bratusch-Marrain (*20*) (*21*) believed spirocid to be the treatment of choice in congenital syphilis of infants and children. He worked out what he considered to be the optimum dosage for infants and made the statement that his material was too small to establish the optimum dosage for the older child but that he thought it would be about the same as for the infant (table 1).

Abt and Traisman (*1*), and Traisman (*205*, *206*) reported on a series of children treated by them with stovarsol. This series increased in number from 22 at the time of their first report to a total of 65 at the time of their last report. These authors used the Bratusch-Marrain treatment scheme. Among the 65 children 21 were under 1 year of age, 22 were between 1 and 6 years old, and 22 were 6 to 12 years old. Twenty-nine of these children received 3 or more courses, and some received as many as 8 courses of treatment. The blood Wassermann and Kahn reactions were positive in all the children before treatment was started. Of the 21 infants treated with from 1 to 7 courses of acetarsone, 4 (19.4 percent) remained seropositive, and 17 (80.6 percent) became seronegative. Of the 22 children between 1 and 6 years of age who were treated with from 1 to 9 courses, 13 (59.1 percent) remained Wassermann positive, and 9 (40.9 percent) became Wassermann negative. Of the 22 children between 6 and 12 years of age who were treated with from 1 to 7 courses, 9 (40.9 percent) remained seropositive, and 6 (27.3 percent) had reversal of the Wassermann and Kahn reactions. The spinal fluid of 31 of the children was examined by means of the Wassermann and Kahn reactions. The findings were uniformly negative. Snuffles disappeared in from 4 to 8 weeks of treatment, generalized maculopapular syphilitic eruption in from 1 to 3 weeks, desquamation of the palms and soles in from 4 to 8 weeks, and splenic enlargement in 6 weeks (in 1 infant, however, splenic enlargement persisted in spite of treatment). Eighteen of the sixty-five children had syphilitic bone lesions, as diagnosed by means of roentgen-ray examination; 13 of these were under 1 year of age. Complete healing took place in all but two following one course of acetarsone. Traisman pointed out that syphilitic bone lesions, especially in infants, have been observed to disappear even without treatment. He also stated that in older children the best results are obtained when bismuth is administered during the 6-week rest period between courses, but he did not mention its use in this series of cases. The length of the observation period following the conclusion of treatment is not given.

Rosenbaum (*172, 173*) has reported on the treatment of a group of children which increased in number from 41 at the time of his first report in 1932 to a total of 395 reported by Rosenbaum and Faulkner (*174*) in 1941. The Bratusch-Marrain dosage system was used (for premature, weak, or ill infants the initial dose was one-half of the usual initial dose). Following a course of acetarsone therapy, 4 weeks of bismuth treatment or mercury with chalk was given to infants, and 10 weeks of heavy metal therapy to older children. According to the authors, these alternating courses should be continued until at least 1 year of treatment has been given, and the blood, spinal fluid, and clinical findings are negative for syphilis. Reexamination including physical examination and blood serologic tests should be done at intervals of 6 months thereafter. The authors state that they have never observed the recurrence of a positive serologic test after all tests had been negative for 1 year. In the 1941 report, a table is presented which shows the number of children in whom serologic reversal (Wassermann and Kahn tests) occurred. Following 1 course of treatment, reversal occurred in 52 children whose ages at the beginning of treatment were as follows: 27 under 2 months, 8 from 2 to 12 months, and 17 over 1 year. Following 2 courses of treatment, reversal occurred in 56 children whose ages at the beginning of treatment were as follows: 11 under 2 months, 25 from 2 to 12 months, and 20 over 1 year. Following 1 year of treatment, reversal occurred in 65 children whose ages at the beginning of treatment were as follows: 6 under 2 months, 10 from 2 to 12 months, and 27 over 1 year (the ages of the remaining children are not given). Following 3 or more years of treatment, reversal occurred in 31 children whose ages at the beginning of treatment were as follows: 2 from 2 to 12 months and 29 over 1 year. The length of the period of observation following treatment or following serologic reversal is not given.

Stern (*199*) gave spirocid, using the dosage scheme of Danzer, to 4 congenitally syphilitic infants varying in age from 14 days to 2 months. All of them had definite syphilitic manifestations. There was symptomatic improvement in 1 case of Parrot's pseudoparalysis in 8 days of treatment. Enlargement of liver and spleen which was present in 2 of these infants was still present after 5 weeks of treatment. Paronychia, present in 1 infant, and coryza, present in 2 infants, persisted for more than 1 month. The Wassermann reaction became negative in 1 infant after 1 course and remained negative during an observation period of 6 months. In another infant it became negative after 3 courses and remained negative during an observation period of 9 months. In the third infant it became negative after 2 courses and again positive after 3 courses and in the fourth infant it became negative after 3 courses. These last 2 infants could not be kept under observation.

Rambar (*168*) gave routine antisyphilitic treatment to premature infants on the basis of the finding of a positive Wassermann reaction in either

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parent. He felt that premature birth of the child of a syphilitic woman was presumptive evidence of syphilitic infection in the infant, even though the mother had been treated during pregnancy. Of 32 premature infants treated with stovarsol (Bratusch-Marrain scheme) 8 received stovarsol only, 7 received stovarsol and mercury and chalk, and 17 out of a group of 43 who had received mercury and sulfarsphenamine during the first year received stovarsol during the second year of treatment. Rambar did not compare the results obtained with these different types of therapy, yet he advised that stovarsol be used because of its ease of administration and because he thought better cooperation of the parents could be obtained with this type of therapy. Snuffles (present in 9 infants, 5 of whom received also mercury and chalk) cleared up in from 4 to 8 weeks on stovarsol therapy; splenic and hepatic enlargement, which was present in 5 infants, disappeared in 3 infants after 1 course of therapy, but in the other 2 splenomegaly persisted after 2 courses of stovarsol had been given. The blood Wassermann and Kahn reactions were found to be negative in all the infants treated with 1 course of stovarsol, or mercury and stovarsol. The author did not state how long these infants were observed after completion of therapy.

Yampolsky (*219*, *220*, *221*, *222*, *223*) has published a number of reports on the treatment of congenital syphilis with acetarsone. He used the Bratusch-Marrain dosage scheme; however, when the Wassermann reaction was found to be positive after 1 course of treatment, no rest period was allowed. In 1934 he reported on a group of 16 Negro children so treated. All of them had positive Wassermann reactions at the beginning of treatment. Following treatment, Wassermann tests were made on 13 of the group and included 5 infants and 8 older children. Among the infants 2 had become seronegative, 2 had remained strongly seropositive, and in 1 the Wassermann reaction had decreased in strength. Among the older children 3 had become seronegative, and 5 had remained strongly seropositive. Following treatment, the spinal fluid of 11 children, including 5 infants, was examined and found to give negative Wassermann and globulin reactions. Some of the fluids showed an increased cell count. Syphilitic bone involvement as evidenced by roentgen-ray changes was found to be present in 13 patients. Clinically most of these patients improved rapidly with treatment. Final roentgenograms were taken in 11 of them. Healing of the syphilitic lesion was found to have occurred in only 1 of these. According to the author, skin lesions improved rapidly, but very little effect of treatment in 3 cases of interstitial keratitis was noted. In a later report Yampolsky advised that in the treatment of older children 6 weekly injections of bismuth should be given during the course of acetarsone therapy or following the course of acetarsone.

In 1941 Yampolsky reported on another series of children treated with acetarsone. Included were 22 infants under 1 year of age and 9 children between 2 and 11 years of age, all of whom received acetarsone exclusively. In 16 of the infants the Kahn reaction became negative and remained so for at least 1 year; in 6 it remained positive. In the older children the Kahn test became negative in more than 50 percent of the cases. Of 16 infants with syphilitic bone changes, 9 showed marked improvement after 3 courses of acetarsone. Of 7 of the older children who had syphilitic bone lesions the bone lesions healed in only one. In a series of 16 children, bismuth was used in conjunction with acetarsone. Seven of these patients had received neoarsphenamine and mercury or bismuth previous to receiving acetarsone and bismuth. In all except one of these cases the positive serologic reaction was reversed. Spinal fluid examination was made on all 47 patients before and after treatment, and no abnormalities were found.

Coppolino (*38*) treated 2 groups of children with acetarsone exclusively, using the Bratusch-Marrain dosage scheme. One of these groups consisted of 10 infants under 1 year of age, all but 1 being from 2 to 4 weeks old. The other group included 10 children from 4 to 12 years of age. Six of the infants were asymptomatic and were treated on the basis of the finding of a positive serologic reaction in the mother. Of the other 4 infants, 1 had condylomata of the vulva, 1 had Parrot's pseudoparalysis of the right arm, and 2 had snuffles. The Wassermann and Kahn reactions were positive in all 10. Two of the infants received 1 course, 4 received 2 courses, and 4 received 3 courses. Within 5 weeks all of the lesions had healed or were markedly improved. The Wassermann and Kahn reactions became negative in 9 infants at the end of the first course; in 1 the Wassermann was reduced in titer, but the Kahn reaction was still 4 plus positive. At the end of a second course all of the infants had negative serologic reactions. In the group of 10 older children 5 were asymptomatic, 1 had interstitial keratitis, 1 had Hutchinson's teeth, 1 had gumma of the left parotid region, and 2 had epilepsy. In 9 of the children both Wassermann and Kahn reactions were positive; in 1, only the Kahn reaction was positive, and strongly so. As a result of treatment the gumma healed in 5 weeks, the interstitial keratitis showed improvement, and 1 of the patients with epilepsy showed improvement. Four of these patients received 1 course, 5 received 2 courses and 1 received 3 courses. The Wassermann and Kahn reactions became negative in 2 (20 percent) and remained unchanged in 8. Coppolino compared the action of acetarsone with that of bismuth in 2 groups of infants. He pointed out that no absolute comparison of the effect of 2 drugs can be made because of the impossibility of studying their action under exactly the same conditions, taking into consideration duration of treatment, degree and virulence of the infection, and number of

cases observed. However, he noted a striking similarity in the action of these 2 drugs. In early infancy lesions healed rapidly on treatment, and the Wassermann reaction became negative, while treatment of children at the end of the first year of life resulted merely in reduction of the strength of the serologic reactions. In 50 percent of the infants treated with bismuth, the reaction became negative at the end of the first course and in 100 percent at the end of the second course. In the older children syphilitic lesions healed as rapidly with bismuth therapy as with acetarsone therapy. On bismuth therapy the Wassermann reaction was reversed in 37.5 percent.

Friedman (*66*) reported on the results obtained with acetarsone treatment (no other drug being given) in 5 infants under 1 year of age. All had clinical and serologic findings of syphilis including Parrot's pseudoparalysis, snuffles, splenomegaly, hepatomegaly, and skin eruption; in addition all showed syphilitic bone involvement as demonstrated by roentgen-ray examination. The mothers, although 3 of them were seropositive, had received no treatment prior to the birth of these children. At first the author used the Tuscherer scheme of dosage, later a modified Bratusch-Marrain scheme in which he gave no rest periods. The Wassermann and Kahn reactions became negative following the administration of from 4 to 15 gm. of acetarsone. Three of these patients were observed until they were from 12 to 15 months of age; the other 2 were lost sight of. Rapid healing of the bone lesions was observed in all 5 infants. The author points out that in some of these patients healing of bone lesions might have occurred without treatment but probably only after a long period.

Fan (*55*) reported on the results of stovarsol treatment of 9 children, using the Bratusch-Marrain scheme. Of these, 8 were from 7 days to 6 months of age and 1 was 12 years old. Seven of the nine had at least 1 course of treatment, and 1 patient had 3 courses. Healing or improvement of the manifestations of syphilis was observed. Of 8 patients in whom serologic reactions were determined before and after treatment, the reaction of 4 became negative after 1 course, 1 became negative after 2 courses, 2 showed improvement, and 1 which had been negative before treatment remained negative. Improvement of syphilitic bone lesions as the result of treatment was also observed.

Arena and Gay (*5*) used the Bratusch-Marrain scheme of acetarsone therapy together with intramuscular bismuth injections in the treatment of 32 children whose ages varied from 1 day to 11 years. Of 15 infants who were included in this series, only 8 received adequate treatment, and of these 6 had reversal of the Wassermann reaction. Clinical manifestations improved rapidly. Roentgen-ray examination of the bones was not made routinely, but in those studied, healing occurred rapidly. Two of three children with interstitial keratitis showed improvement in 9 weeks and

healing in 6 months of treatment. Arena and Plummer (*6*) recommended acetarsone for the treatment of congenital syphilis.

Paddle (*160*) used acetarsone according to the Bratusch-Marrain scheme in the treatment of 29 mental defectives with congenital syphilis. Both sexes and all ages were included. He divided them into 2 groups. Group 1 consisted of 19 patients whose cerebrospinal fluids were normal. Of 17 of these with positive Wassermann reactions before treatment, 8 became negative, 7 had less positive reactions, and 2 remained definitely positive. Group 2 consisted of 10 patients with abnormal cerebrospinal fluids (3 with juvenile paresis, the others with meningovascular syphilis). Of 9 with positive blood Wassermann reactions only 1 became negative after treatment. The cerebrospinal fluid Wassermann reaction of 7 was positive before treatment. Following treatment, 2 became negative and 4 reduced in strength; 1 which had been negative before treatment became slightly positive after treatment. The majority of these patients had received 6 to 7 courses over a period of a little more than 2 years. As the result of treatment 27 showed physical and 23 showed mental improvement. A syphilitic ulcer healed in 10 days, interstitial keratitis (present in 1 patient) healed in 2 months of treatment.

Smith, Fried and Everhart (*191*) used a modified Bratusch-Marrain scheme in the treatment of 23 infants under 1 year and 10 children over 1 year of age. They gave 0.005 gm. per kg. per day for 2 weeks, 0.010 gm. per kg. per day for 2 weeks, 0.015 gm. per kg. per day for 2 weeks, and 0.02 gm. per kg. per day for 12 weeks. This was followed by a rest period of 1 month during which mercury with chalk was given. The Wassermann reaction was determined after a course of treatment was completed. If negative, another course was given, and if the Wassermann reaction following this course was also negative, a final course was given. The parents were advised to return the child to the clinic for a check-up every 6 months over a period of 2 years. Following treatment, 19 (82.6 percent) of the 23 infants became seronegative and 4 remained seropositive. Of those who became seronegative 8 required more than 1 course to bring about Wassermann reversal. In general the younger infants had more florid evidences of syphilis; 8 had Parrot's pseudoparalysis, 6 had snuffles, and 1 had marked hydrocephalus. Improvement of Parrot's pseudoparalysis was noted after 2 weeks of treatment and complete disappearance after 1 month. Complete healing of syphilitic bone involvement usually was noted at the end of 1 course. Of the 10 older children, 5 (50 percent) became seronegative after 1 or more courses and 5 remained positive.

Korman, Smith and Abt (*101*) also modified the Bratusch-Marrain system of dosage by administering bismuth salicylate from the tenth through the fifteenth week; in the sixteenth week, acetarsone 0.01 gm. per kilogram was given daily; from the seventeenth week through the twenty-

fourth week the daily dose of acetarsone was 0.02 gm. per kg. and from the twenty-fifth to thirtieth week bismuth salicylate injections were given. The dosage of bismuth salicylate was: 6 months of age ⅛ cc.; 6 months to 1 year, ¼ cc.; 1 year to 4 years, ½ cc.; 4 to 8 years, ¾ cc.; 8 to 12 years, 1 cc., and 12 years, 1½ cc. A total of 98 infants and children were treated with this scheme, 70 of them being under 1 year of age. There were 28 who received 3 or more courses and 31 who received only 1 course. Serologic reversal occurred in 25 after the first course, in 15 after the second course, and in 3 after the third course of stovarsol and bismuth, a total of 43 percent. These authors stated that they used the continuous method of treatment for at least 2 years in each case of early or late asymptomatic congenital syphilis.

Nabarro (*142*) in a recent publication pointed out that the dearth of reports on the use of stovarsol in Great Britain is presumably prima facie evidence that the drug has found little favor among British venereologists and pediatricians. He studied a group of institutionalized children (residential unit for congenital syphilis) during a period from 1933 to 1939. In giving stovarsol therapy he used a modified Bratusch-Marrain scheme of dosage by means of which 5.5 gm. per kilogram of body weight of stovarsol was given per year. Blood and spinal fluid tests were usually done before treatment was started, the blood Wassermann reaction being repeated after each course and the spinal fluid test only if it had been positive in the first test. After 3 negative blood tests were obtained, treatment was usually stopped, but was resumed if serologic relapse occurred. Follow-up after treatment had been stopped was done every 3 months for 1 year, every 6 months for another year, and every year for as long as possible.

Altogether 140 patients were treated, including adults. There were, however, only 43 patients (all children) who received "mainly" or only stovarsol. The author pointed out that this group constitutes the only cases which can be utilized in the evaluation of stovarsol for the treatment of congenital syphilis.

A careful analysis of the details which the author gives for each of these 43 cases shows the following:

Among the group of 43 children treated, 31 were 1 year old or less (7 were 1 month or less of age; 2 were 2 months; 15 were 2½ to 6 months and 7 were 7 months to 1 year of age), and 12 were over 1 year of age (5 were 2 to 4 years old and 7 were from 4 to 10 years old).

Of the 7 who were 1 month or less of age, all had manifestations of syphilis and strongly positive Wassermann reactions; 4 of them died at from 2 weeks to 6 weeks after treatment was started (after 0.016 to 1.14 gm. stovarsol), one death being due to diarrhea and the cause of the other 3 deaths being obscure. Three were apparently cured (2 of these also received either bismuth or mercury) after from 3.0 to 34.0 gm. of stovarsol

(orarsan). These 3 were observed 3½ months, 15 months, and 2 years, respectively, following the conclusion of treatment.

Of the 2 who were 2 months of age, 1 had and 1 did not have manifestations; both had strongly positive Wassermann reactions. The one with manifestations died of bronchopneumonia after 1 week (0.15 gm. stovarsol), the other received 1 injection each of sulfarsphenamine and bismuth, then a total of 63 gm. stovarsol. The Wassermann reaction reversed to negative at 7 months and remained negative for an observation period of 8 months following treatment.

Of the 15 who were 2½ to 6 months of age, 10 had and 5 did not have manifestations; all had strongly positive Wassermann reactions. Five (33 percent) died—1, meningitis; 1, whooping cough; 3 (20 percent), drug intoxication—in from 1 to 10 months after treatment was started (0.9 to 13.0 gm. stovarsol), 3 left treatment before the results could be evaluated. Of the remaining 7 who were treated with apparent success, only 2 received stovarsol alone, 2 received 1 injection of sulfarsphenamine preceding stovarsol therapy, and 1 received 4 injections of acetylarsan preceding stovarsol therapy; 1 received bismuth and another mercury in addition to stovarsol. The Wassermann reaction reversed in from 2½ to 10 months of treatment. The observation periods after treatment had been stopped were none, 1½ months, 3 months, 4 months, 5 months, 1 year and 9 months, and 4 years and 2 months, respectively.

Of the 7 who were 7 months to 1 year of age, 5 had and 2 did not have manifestations; all had strongly positive Wassermann reactions. There was 1 definite treatment failure which occurred in a 1-year-old child whose Wassermann reaction became negative at the age of 16 months (after 1.2 gm. sulfarsphenamine and 29 gm. stovarsol) and then relapsed to positive at the age of 5 years. It was still positive at the age of 7 years, following an additional 58 gm. stovarsol and mercuric iodide but reversed to negative when the child was 8 years old and had received a total of 173 gm. stovarsol. Of the other 6 who were apparently cured, only 1 received mercury therapy in addition to stovarsol; the other 5 received only stovarsol. The Wassermann reaction reversed in from 6 to 18 months and after a total dosage of from 48 to 123 gm. stovarsol. The observation periods after treatment was concluded were none (2 patients), 1½ months, 2 years and 2 months, 4 years, 4 years and 1 month, respectively.

Of the 5 children whose ages were 2 to 4 years, 2 did not have and 3 did have manifestations of syphilis; all had strongly positive Wassermann reactions. One child aged 1 year 11 months at the beginning of treatment had a positive spinal fluid Wassermann reaction at 2 years which became negative at 2 years 9 months (sulfarsphenamine 0.95 gm., bismuth, and stovarsol 77 gm.). The blood Wassermann reaction in this case became negative at 3 years 3 months, but the child was not observed following

treatment. The other 4 were apparently cured after a total of from 116 to 236 gm. stovarsol (2 also received mercuric iodide). The Wassermann reaction reversed in from 22 to 28 months of treatment. The observation periods after treatment had been stopped were 5 months, 2 years and 8 months, 3 years and 8 months, and 5 years and 6 months, respectively. The child who was observed for 5 years and 6 months had had a positive spinal fluid at 3½ years which became negative with 6 months of stovarsol treatment.

Of the 7 children whose ages were from 4 to 10 years, 5 did not have and 2 did have manifestations (1 saddle nose, 1 Hutchinson's teeth). All had strongly positive Wassermann reactions. Four received bismuth and mercuric iodide in addition to stovarsol. There were 2 and possibly 3 treatment failures in this group: One 7½-year-old child without manifestations still had a positive blood Wassermann reaction at 9 years of age (53 gm. stovarsol) at which time she was lost from observation, and another 7-year-old child without manifestations still had a positive Wassermann reaction after 9 months of treatment. A third child was started on treatment when she was 5½ years old (stovarsol, bismuth and mercuric iodide). Her blood Wassermann reaction became negative at 7½ years but was strongly positive again at 8¾ years and negative at 10 years. She was not observed following the conclusion of treatment. Four children were apparently cured after from 25 to 272 gm. stovarsol (2 also received considerable bismuth).

The blood Wassermann reaction reversed in from 3 to 30 months, and the observation periods following treatment were 2 years 3 months; 3 years 4 months; 3 years 5 months; and 3 years 10 months, respectively.

Results Obtained with High Dosage–Intermittent Scheme

Klaften (*95*, *96*) recommended the use of stovarsol only in cases where it is absolutely impossible for the mother to bring her child to the clinic for arsphenamine treatment, which he considers unquestionably superior to stovarsol. In 1927 he reported the results of treatment of 6 infants who had either a positive Wassermann reaction or positive spirochete finding in the cord or both. None of them had any manifestations of syphilis. Altogether 4 had positive Wassermann reactions. He gave the drug every 2 days and protiodide powders on alternate days; the dosage per 3-month course was 15 gm. As a result of treatment the Wassermann reaction became negative in 3 and remained continuously positive in 1; all of them remained free of manifestations. In 1928 he reported on the prophylactic treatment of infants with negative findings whose mothers were syphilitic. One of these infants developed a syphilitic skin eruption and a positive Wassermann reaction during the course of treatment, and these positive

findings continued to persist in spite of intensive spirocid treatment. When, however, arsphenamine was given instead of spirocid, the lesions disappeared, and the reaction of the blood became negative. For this reason Klaften thereafter used spirocid only in those cases in which a combined course of neoarsphenamine and calomel or bismogenol could not, for some reason, be carried out.

Von den Steinen (*198*) treated (7 days treatment followed by 7 days rest in a dosage of 10 to 15 gm. in 3 months) a total of 10 children with spirocid; 5 were under 2 months, 1 under 3 months, 1 was 1 year, 2 were 3 years, and 1 was 8½ years of age. The infant who was under 3 months of age died of a staphylococcus skin infection on the seventh day of treatment. All of the other 9 children had strongly positive Wassermann reactions and 5 of them had typical syphilitic skin manifestations. The skin was observed to improve in 3 to 4 days, Parrot's pseudoparalysis in 17 days. One of the 3-year old children had acquired syphilis, and in this child the manifestations disappeared in 3 weeks. With the exception of 1 child (a 3-year-old child with congenital syphilis) the Wassermann reaction reversed to negative in 3 to 4 months. This author mentions that bismuth was given in addition to spirocid to 2 children but does not definitely state whether any of the others also received bismuth.

Hom (*82*) used the method of von den Steinen in the clinic-polyclinic treatment of 80 children with congenital syphilis. Of these, 64 received spirocid only, 12 spirocid and bismuth, and 4 spirocid "in another combination." Before treatment was given 57 of these children were seropositive; 23 were treated prophylactically. Of the 80 who were started on treatment 37 were lost before the end of the first course, 14 of these having died. Only 1 of these deaths was attributed to the toxic action of the drug. Of the 43 who continued treatment, 24 received 1 course, 11 received 2 courses, 4 received 3 courses, and 4 received 4 courses. Of the 57 originally seropositive children the serologic reaction following treatment could be evaluated in only 33 because 24 of them had discontinued treatment before 1 course had been given. In 7 of these the Wassermann reaction became negative after 1 course, 6 of these 7 being infants under 1 year of age and the seventh having had previous treatment. Three others were found to have reversal of the Wassermann reaction after further spirocid-bismuth therapy. It was found, however, that 50 percent of the children who were still strongly seropositive after the first course were less than 1 year of age. The size of the dosage did not seem to be of importance; negative Wassermann reactions having been obtained in cases which received total doses of 7 to 13 gm. Another group of 28 children were treated only as outpatients. Of these, 17 were seropositive before treatment; 4 of these were lost before the first course was completed. Of the remaining 13, 2 became seronegative after the first course

(spirocid only) but one of these again became seropositive at the beginning of the second course. With further treatment 1 other patient became seronegative; the others remained seropositive. Therefore, out of the entire group only 27 percent became seronegative as the result of treatment. The author points out that this percentage is very low in comparison to the results obtained with combined neoarsphenamine-bismuth or neoarsphenamine-mercury treatment with which 80 percent of reversals of the Wassermann reaction can be obtained. In regard to the manifestations of syphilis, skin lesions began to heal after the administration of 1 to 2 gm. spirocid, syphilitic coryza was often still present after 1 course, although it was usually improved and splenomegaly and hepatomegaly often persisted throughout the first 2 courses. The author concluded that the only advantage of spirocid treatment is its peroral administration and questions this apparent advantage because of the fact that parents are often careless and irresponsible so that they cannot be entrusted with the treatment. He saw no reason for giving it in place of neoarsphenamine and stated that if myosalvarsan should prove effective, this drug together with bismuth or mercury would constitute the treatment of choice in congenital syphilis.

Wegner (*211*) used the Spiethoff scheme of spirocid dosage (7 days treatment, 4 to 7 days rest; total of 20 to 25 gm. in 6 months) and advised that if during the course of treatment the serologic reactions are not sufficiently affected, spirocid should be discontinued and bismuth given in place of it, and if bismuth does not produce the desired results, then myosalvarsan should be tried. If myosalvarsan also is not effective then treatment should be discontinued for 1 year and resumed after that. For children from the third year of life on, Spiethoff recommended arsphenamine instead of spirocid.

In Müller's (*137*, *138*, *139*, *140*) opinion the results obtained with spirocid in the treatment of children over 2 years of age are not satisfactory; he therefore recommended that in these children combined neoarsphenamine and calomel treatment be given instead of spirocid. His spirocid treatment scheme (table 1) applied only to infants under 2 years of age. He gave only 1 course which extended over a period of 3 months. The Wassermann test was made 10 days after treatment had been stopped, and several more tests were made at weekly intervals after that. Acute manifestations were observed to disappear under spirocid treatment but not as rapidly as with neoarsphenamine-calomel treatment. Out of a total of 62 children under 2 years who were treated (*138*), all became clinically negative, and 60 became seronegative. Of these, 21 were followed for 3 months, 16 for 6 months, 2 for 9 months, 5 for 12 months, 15 for 18 months, and 3 for 2 years. The 2 positive serologic reactions occurred in children observed for 3 and 6 months respectively. The author also reported on the fate of 38

infants whom he personally studied. Of these, 3 died in the first week, before treatment was given; 5 died during or after treatment; 3 did not complete treatment; 2 had already been treated and were not further treated; 1 received neoarsphenamine elsewhere soon after spirocid therapy. Therefore only 24 remained for evaluation of results. All of them were seronegative at the time of the last observation—4 at 3 months, 4 at 6 months, 2 at 9 months, 2 at 12 months, 9 at 18 months, and 3 at 2 years. Müller offered no explanation in regard to the cause of death in 5 infants (14 percent) who died during or after spirocid treatment.

In 1933 Müller (*139*) reported on the results of treatment of 50 children with a single course of spirocid. Of this number 39 could be followed for a period of 5 years after treatment, all of them remaining free from recurrences and 37 of them remaining seronegative. In 1 child the Wassermann reaction was negative for 2 years and then became doubtfully positive; in another child the Wassermann reaction became definitely positive after 1 year. In 1938 he stated that he considered spirocid to be the treatment of choice in the infant. He advised that all infants whose mothers did not receive sufficient prophylactic therapy during pregnancy should be treated prophylactically with spirocid.

Meyer (*132*) used the Müller dosage scheme in the treatment of 60 children. All except 1 became seronegative following treatment. Wassermann reversal was observed after 15 to 20 gm. of spirocid, but as a rule not until after the administration of 30 gm. Skin manifestations disappeared in about 8 days, snuffles in 3 weeks. Splenic enlargement persisted for a longer period.

Huber (*83*) treated 16 infants and 7 children (ages 1¾ years to 10 years) with spirocid according to his own scheme (spirocid every 2 days, total of 20 to 30 gm. per course). Among the infants, skin manifestations disappeared after 8 to 14 days and at the latest after 21 days and the mucous membrane lesions in about 3 weeks. Spleen and liver decreased definitely in size after 4 to 8 weeks. Parrot's pseudoparalysis disappeared in 8 to 10 days. Among those infants who received a course of 22.5 gm., 2 still had positive Wassermann reactions at the end of the course whereas all of those who had received 30 gm. had negative reactions at the end of a course. The Wassermann reaction reversed to negative in only 1 of the older children, namely in the child who was less than 2 years of age. Two of these children received 2 courses of spirocid, but the Wassermann reaction remained positive. Huber recommended that bismuth be given simultaneously with spirocid therapy since spirocid alone does not seem to have much effect on the Wassermann reaction.

Kundratitz (*109*) first tried the Oppenheim dosage scheme but found the dosage too low to have any appreciable effect on the Wassermann reaction or on the manifestations. Even with increased dosage (8 to 10

days treatment followed by several days rest; 15 to 20 gm. per course) the results were not as good as could be obtained with neoarsphenamine. Of 15 children treated, 9 became seronegative after 1 course and 6 remained positive after 1 course; 3 remained positive after several courses. It was also found that serologic reactions which had become negative after spirocid treatment were more apt to return to positive again than the negative reactions resulting from neoarsphenamine therapy.

Eckhardt (*48*) used his treatment scheme (4 to 10 days treatment followed by 4 days rest; 12 to 15 gm. in 12 weeks) in 33 infants under 2 years of age. Six of these were not observed for a sufficient period of time, and 5 died during or shortly after the course of treatment. The other 22 infants completed at least 1 course of treatment with the result that in 17 the Wassermann reaction became negative and in 5 it remained positive. The best results were obtained in the youngest children. Eleven of the twenty-two received a second course of spirocid, including the 5 who had remained seropositive after the first course. Of these 5, 2 remained seropositive in spite of 2 and 3 more courses, 2 became negative after further spirocid, and 1 after myosalvarsan. These 3, who were observed from 6 months to 4 years, remained negative. In 6 children who had already been treated unsuccessfully with other antisyphilitic drugs, negative Wassermann reactions were obtained with spirocid; 2 of these children required 2 courses to bring about this result.

Mettel (*130*) reported on the treatment of 4 children aged 6 to 12 years. No standard dosage was given but as a rule a total dosage of 0.25 gm. stovarsol per kilogram was the amount of treatment given per course. At first 0.25 gm. was given every other day during the first week. Later, if the drug was well tolerated, 0.25 gm. was given every day for 3 days followed by a rest period of 2 days. The children treated all had bone lesions and strongly positive Wassermann reactions. The Wassermann reaction remained positive in all of these children, including 1 who received stovarsol for a period of 1 year. The bone lesions healed in all of them.

Nedelmann (*143*) reported on the results of spirocid treatment of 18 infants. The dosage scheme used was that of Müller. Spirocid was the only drug given. In this group 11 were less than 3 months of age, 5 were 3 to 6 months old, and 2 were between 6 and 9 months old. Of these, 17 became seronegative after 1 course of treatment. One infant in the 6 to 9 month age group was still seropositive after a total dosage of 90 gm. spirocid but became seronegative after a second course of 30 gm. Fourteen of the treated children were followed for from 3 to 26 months (4 for 3 months, 3 for 9 months, 2 for 12 months, 4 for 20 months, and 1 for 26 months) and during this time remained Wassermann negative and free from recurrences.

Joseph (*90*) treated 14 children whose ages were fairly evenly distributed over the years 1 to 18 (except 1 child 4 months old). He gave intra-

muscular injections of bismuth in addition to stovarsol therapy. He administered stovarsol every other day, beginning with 0.125 gm. and increasing it by 0.125 gm. at every dose until a dosage of 0.5 gm. was reached on the seventh day. This dosage was maintained and was given every other day. The total dosage administered varied between 4 and 40 gm. Five of the children had received no previous antisyphilitic therapy. The Wassermann reaction which was positive in 4 of these became negative on stovarsol-bismuth therapy. The other 9 had apparently had no previous antisyphilitic therapy. The Wassermann reaction was reversed to negative in 2, reduced in 3 and remained strongly positive in 4 of these children. The length of the observation periods is not stated.

Results Obtained with High Dosage–Continuous Scheme

Krombach (*107*) treated (10 to 15 gm. spirocid plus 5.7 gm. bismuth salicylate or 15 to 30 gm. spirocid alone in 3 to 4 months) 12 infants, all except 1 of which were between 3 and 8 weeks old (1 aged 4 months) and also 3 children from 1½ to 2 years of age who had already received antisyphilitic treatment. She did not definitely state how many of the children received bismuth salicylate and how many received spirocid only, except to say that when toxic symptoms were noted spirocid was discontinued, and bismuth salicylate injected once or twice before spirocid therapy was resumed. Two of the children died during treatment; of the remaining 13 all but 1 had a negative Wassermann reaction after the first course of treatment. Skin manifestations of syphilis disappeared in about 4 weeks and spleen and liver enlargement in about 8 weeks. The author pointed out that further studies and, above all, longer periods of observation of children who have been treated with spirocid would determine the relative value of spirocid in the treatment of congenital syphilis.

Soldin and Lesser (*193*) and Lesser (*112*) reported that in many children who were treated with spirocid alone (30 to 50 gm. in 3 months), up to the point when a Wassermann reversal occurred, reexamination at a later period showed the Wassermann reaction to have become again positive, without any other signs of syphilis being present. This led them to develop their more intensive dosage scheme. According to this scheme the children received as much spirocid after the Wassermann reaction had reversed to negative as it took to bring about the reversal; this was never less than 30 gm. The Wassermann reaction was more apt to reverse when syphilis was treated early. In about half of the infants treated, reversal occurred after 15 gm. and in the other half after 20 to 50 gm. Fourteen infants (ages 2 weeks to 5 months) were observed for 2 years after treatment had been stopped. Both blood and spinal fluid were negative at the end of this time.

Menne's (*129*) dosage for 18 infants treated by her varied from 0.03 to

0.5 gm. given in divided doses during the day; the treatment period varied between 54 and 175 days, and the total amount of spirocid administered varied between 7.5 and 40 gm. Of the 18 infants, 9 had positive Wassermann reactions, 6 had negative Wassermann reactions but definite symptoms of syphilis, and the mother had a positive Wassermann reaction; 2 infants had no symptoms and had negative Wassermann reactions. They were treated because of a positive Wassermann reaction in the mother. The reaction reversed to negative in 8 infants, the ninth one having died during the first few days of treatment. Reversal occurred between 44 and 162 days with a total of 1.56 to 33 gm. of the drug. The younger the infant, the smaller was the amount of treatment required to bring about the result. Skin manifestations disappeared in 2 to 22 days, average 9 days; bone changes, present in 7 infants, healed in from 2 to 6 months; 1 case of Parrot's pseudoparalysis healed in 11 days. Enlarged liver and spleen returned to normal size in 2 to 6 months. v. Mettenheim (*131*) reported on this same group of children.

Bamberger (*10*) used the Soldin and Lesser dosage scheme in the treatment of 26 infants with skin and visceral manifestations of syphilis. The amount of drug needed to bring about healing varied with the individuals treated. Of the 26 treated, 8 died, 9 still had positive Wassermann reactions at the end of the period of hospitalization, and 9 had negative Wassermann reactions. He compares this group to a group of 21 infants who were treated with arsphenamine. Of this group 12 died, 4 still had positive Wassermann reactions at the end of their stay in the hospital, and 5 had negative Wassermann reactions. Reversal of the Wassermann reaction usually occurred after a total of 15 to 31 gm. of spirocid, but in 1 child the reaction was still positive after 93 gm.

Tuscherer (*207*) using his own dosage scheme (table 1) administered spirocid to all the congenitally syphilitic children observed in his clinic in a period of 2 years. The majority received only spirocid, a small number received in addition protiodide or intramuscular injections of mercury. In his report he stated that several of these children were followed for a year or more and that spirocid therapy is comparable to arsphenamine-mercury in regard to the results produced. But he gave no details whatsoever except the outline of dosage. He merely stated that in many cases the Wassermann reaction became negative after the first course and that in these cases a second course is given to maintain the good effect produced. Clinical symptoms were usually observed to disappear in the first 3 to 4 weeks; skin eruptions after 10 to 12 days.

Kiss (*93*) used his method (15 to 20 gm. in 3 months) of spirocid therapy in 21 infants of whom the youngest was 4 weeks, the oldest 12 months of age. Treatment could be continued in 18 of these infants. All had positive serologic reactions as well as manifestations of syphilis. Maculopapular

exanthemata disappeared in 7 to 10 days, condylomata in 14 days. Enlargement of the spleen persisted the longest. The Wassermann reaction became negative in 7 of the infants. Reversal occurred following a total dosage of 5.5 to 12 gm. average 9 gm. spirocid. Two of the infants had received intramuscular bismuth injections in addition to spirocid. The period during which they were observed following treatment is not given.

Jochims (*89*) reported on the results of treatment (30 to 50 gm. in 3 to 4 months) of 30 hospitalized infants in the Kiel children's hospital, who were observed for a period up to 2½ years. He found that for the treatment of manifest infant syphilis, as a rule, only a single course of spirocid (30 to 50 gm.) was required. Ambulant treatment with spirocid was found to be unsuccessful since the relatives did not feed the tablets regularly to the children, and control on the part of the physician was impossible. No other antisyphilitic drug was used. With only one exception the Wassermann reaction became and remained negative. Jochims pointed out that in severe lethal cases of visceral syphilis this type of treatment is no more successful than other types of treatment and that a final evaluation of permanent results would be possible only after decennia.

Maxwell and Glaser (*126*) developed their own dosage scheme, after first using that of Tuscherer, because of the report by Martin of 2 cases of paralysis in infants who had been treated according to the Tuscherer scheme. Maxwell and Glaser treated a total of 10 infants, 5 of whom were syphilitic while 5 others may or may not have been syphilitic. Their policy was to treat all babies of syphilitic mothers, starting treatment shortly after birth. Definite signs of syphilis were present in only 2 of the infants treated. All 10 had a full course of treatment, and the Wassermann reversed to negative in all of them. The length of the observation period is not stated. Acetarsone was also used in the treatment of 9 children from 1¼ to 10 years of age but for insufficient time to permit any conclusions (2 to 8 months). The authors stated, however, it seemed rather definite that, in common with other methods of treatment, the Wassermann reaction is not so easily influenced as in infants under 1 year of age. The older children also received bismuth. Interstitial keratitis, which was present in 1 of the children treated improved greatly on acetarsone therapy, before bismuth had been started.

The most outstanding study of the treatment of congenital syphilis with acetarsone is that of Pillsbury and Perlman (*161*, *162*). By means of the dosage scheme of Maxwell and Glaser a total of 196 patients were treated with acetarsone. Of this number 187 had a definite diagnosis of congenital syphilis; 87 were followed for more than 3 years after treatment was started, 116 for over 2 years, and 145 for over 1 year; 83 percent of the patients were Negroes. The Kolmer complement fixation and Kahn tests were done at the beginning and end of each course of treatment. In gen-

eral when a completely negative reaction was obtained, one more course of acetarsone was given and treatment then discontinued, provided no evidence of clinical or serologic relapse was noted. Acetarsone treatment was started cautiously (initial dosage reduced to half) in premature infants, in those severely ill from syphilis, and in infants with syphilis of a vital organ. Acetarsone was used alone so that it might be properly evaluated. In regard to the clinical effects of acetarsone, these authors noted disappearance of spirochetes from the cutaneous lesions after 72, 96, and 120 hours respectively in 3 patients whose lesions were thus observed. Healing of cutaneous lesions occurred in 3 to 4 weeks, rarely in 2 weeks. The authors regard the effect of acetarsone on infectious lesions as distinctly slower than that of arsphenamine and certainly no more rapid than that of an insoluble bismuth salt. Of 12 cases of definite roentgenologic evidence of bone involvement in which reexaminations were made, 11 showed marked to complete healing following treatment. In 1 patient with syphilitic osteitis of the skull no change in the condition occurred. The effect of acetarsone on interstitial keratitis was disappointing. In 5 cases the course of the active lesion was prolonged and involvement of the other eye was not prevented. In 3 cases marked corneal nebulas and significant decrease in vision were the end-results. Late clinical relapse after acetarsone treatment was not observed. Clinical progression of the disease in spite of treatment occurred in 8 cases. Serologic reversal (both Kolmer and Kahn tests negative) was obtained in 70 percent of children under 6 months of age. The authors compare this result with that obtained by Smith (*192*) in his series of congenitally syphilitic children treated with arsphenamine and heavy metal. Smith obtained 94.2 percent of reversals in children whose treatment was begun before the age of 6 months and given regularly during the first year. With intermittent treatment his percentage was approximately 80 and with very irregular treatment, 70. In children over 6 months of age Pillsbury and Perlman found only 36 percent of serologic reversal following acetarsone therapy. They compare this to Smith's finding of 29 percent obtained among patients over 2 years of age. To 47 patients arsphenamine and a bismuth or mercury compound were also given. In most of these administration of acetarsone followed the other types of therapy. Of 7 patients for whom this treatment was started before the age of 6 months, all became seronegative. Among 40 patients whose treatment was started after the age of 6 months, 30 percent became seronegative. Spinal fluid examinations were made in 103 of the patients and the incidence of neurosyphilis found to be slightly less than 4 percent. The average period during which the patients were followed after treatment was begun was 2.8 years. Among 87 patients observed for over 3 years after acetarsone therapy, only 1 instance of serologic relapse of the blood was noted. No instance of clinical relapse of a lesion

not present when treatment was started was observed. A comparison was made between the attendance at the clinic of patients who received injection treatment and those who received acetarsone. It was found that the percentage attendance of patients receiving injection therapy and acetarsone, respectively, was exactly the same, namely 51 percent.

Davidson and Birt (*44*) treated 23 children most of whom had late congenital syphilis with stovarsol according to the Maxwell and Glaser scheme. Of these 23, 13 had been previously treated by means of intravenous and intramuscular injections. Following 2 years of stovarsol treatment 14 blood reactions reversed to negative, and 2 were reduced to doubtful.

Van Dermark (*46*) used stovarsol only in the treatment of 90 children. The Maxwell and Glaser dosage system was used and at least one course given to all the children, following which a serologic test was made. The course of stovarsol treatment was followed by a rest period of 4 weeks during which mercury rubs were given daily. After 3 such courses a rest period of 3 months was allowed and then another course of stovarsol given. This was followed by 6 months' rest period. No further treatment was given unless it was found that the Wassermann reaction had again become positive or symptoms had recurred. Twenty other patients were also treated with stovarsol but after they had been previously treated with other arsenicals. Among the 90 patients 44 were under 1 year of age, 15 were 1 to 4 years, and 31 were over 4 years of age. All infants whose syphilitic mothers had received inadequate treatment during pregnancy or in whom the history of the mother was very suggestive of syphilis were treated, regardless of the cord Wassermann reaction or the reaction of the infant's blood. In the group under 1 year of age 84 percent became serologically negative, and 16 percent remained positive. If the group of 17 infants whose diagnosis of syphilis was made only on the mother's history is taken out, 74 percent became seronegative. In the group from 1 to 4 years of age and in the group of more than 4 years of age only 20 percent became seronegative as a result of stovarsol treatment. One instance of serologic relapse occurred; this was in an infant whose Wassermann reaction had become negative after 6 courses and who returned after 6 months' rest period with a positive Wassermann reaction. These authors found that stovarsol treatment was not very effective after one or more years of therapy with other arsenicals had failed to reverse the Wassermann reaction. Twenty such cases were treated with as many as 8 or 10 courses of stovarsol and only 2 of these subsequently had a negative Wassermann reaction. It was found that lesions involving the skin, mucous membranes, bones and joints responded most rapidly to stovarsol, whereas in interstitial keratitis the response to treatment was much slower, and often bismuth had to be given before the lesion healed completely.

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Mahler (*122*) treated 25 congenitally syphilitic infants under 2 years of age with spirocid according to the Tuscherer dosage scheme. Of these 10 (40 percent) were cured (became Wassermann negative), 2 after 1, 7 after 2, and 1 after 3 courses of treatment; 4 (16 percent) were not cured, and 11 (44 percent) died.

Of a group of 15 infants under 2 years of age treated with acetarsone (Maxwell and Glaser scheme) and reported by Lyon and Seymour (*121*) and by Lyon and O'Neil (*120*), 10 (67 percent) had Wassermann reversals and were free of symptoms by the end of the first year. With sulfarsphenamine and neoarsphenamine therapy, 15 (79 percent) of a group of 19 infants similar results were obtained. In older children, 2 to 15 years of age, the results were less satisfactory since negative serologic tests and freedom from symptoms occurred in only 13 (34 percent) of a series of 38 children treated with acetarsone and in 13 (21 percent) of 64 children treated with other arsenicals. Routine treatment was given to a group of newborn infants whose mothers were syphilitic and who had not received adequate antisyphilitic treatment during pregnancy. The infants were given daily mercury inunctions during the first week of life, and the mothers were instructed to continue this treatment at home during the first 6 weeks. All but 5 of 36 infants so treated returned to the clinic and were started on acetarsone treatment before they had reached the age of 2 months. In 22 of 27 of these infants whose cord blood was tested by means of the Wassermann reaction the reaction was found to be positive; symptoms suggestive of syphilis occurred in 11 of these infants. These manifestations, consisting of snuffles and skin lesions, disappeared in from 1 to 5 weeks. After 1 year of treatment all the patients but one (started on treatment at 8 months of age) were free from symptoms and had negative serologic reactions. Ten of the patients were observed for 1 to 3 years after treatment was stopped, and they remained free from symptoms of syphilis and continued to have negative serologic reactions. In an older boy, interstitial keratitis developed 1 week after acetarsone therapy was started. Bismuth was then added to the treatment and the lesion healed.

Continuous Versus Intermittent Dosage

Bielenstein (*17*) treated a total of 24 infants. Of this number 14 received intermittent treatment according to the scheme of v. den Steinen whereas in the other 10 infants the 7-day rest periods following the 7 days of spirocid administration were omitted and treatment was continuous. In other words, both groups received the same amount of total treatment but those in the second group received it in half the time. Treatment was not completed in 4 infants of the first group since the parents took them home before this. All of these 4 still had positive Wassermann reactions following a period of treatment of less than 3 months. Clinical symptoms dis-

appeared as rapidly on intermittent as on continuous treatment. The Wassermann reaction became negative following the first course of intermittent therapy in 80 percent of infants and after the first continuous course in only 30 percent; a second continuous course was required to bring about results comparable with those obtained with only one course of intermittent therapy. Skin lesions were observed to fade after several days of treatment and to disappear completely in 4 weeks, coryza in 3 to 4 weeks, enlargement of the spleen in 3 to 7 weeks. Parrot's pseudoparalysis, present in 3 infants, was healed in 12 days to 5 weeks of treatment. In 3 infants syphilitic nephrosis improved on spirocid therapy.

Baumbach (*77*) reported on a continuation of the work of Bielenstein. His report deals with the results of spirocid treatment of 61 infants. Ten infants were treated continuously and 5 intermittently, as outlined by Bielenstein. In addition, 28 infants treated with the intermittent scheme received mercury inunctions during the 7-day rest periods which followed the 7 days of treatment. In none of the infants of the first group (continuous treatment) did the Wassermann reaction become negative after the first course; all were negative after the second course. In the 5 infants of the second group 3 still had a moderately positive Wassermann reaction after the first course (intermittent therapy) whereas 2 had negative reactions. Four of these infants received a second course following which the Wassermann reaction was negative and remained so. There were 28 infants in the third group which received both spirocid and mercury inunctions. Following one course of treatment the Wassermann reaction became negative in 19 (68 percent), remained strongly positive in 5, and decreased in titer in 4. It was observed that the younger the infants were the more easily could the Wassermann reaction be reversed by treatment. The author, on the basis of these results, advised that combined spirocid-mercury inunction therapy, using the intermittent scheme should be used and treatment started as early as possible.

A few other authors have reported briefly on their experience with acetarsone in congenital syphilis. Maillet (*123*) treated 120 children in whom congenital syphilis was suspected but in whom definite signs were lacking. In this group the Wassermann was positive in 43 cases. Mercury by mouth was used together with stovarsol. Four days of stovarsol treatment were followed by 3 days of rest, a course of treatment lasting 6 weeks. The dose was 0.02 gm. (initial dose half this amount). Of the 43 positive Wassermann reactions 17 became negative after the first course of treatment. In this author's opinion treatment should be given for 3 to 4 years and should consist of 4 courses the first year, 3 the second, and 2 in the third and fourth years.

Martin and Vierkotten (*125*) used prophylactic spirocid treatment in a group of 117 illegitimate infants, beginning treatment on the third day of

life. Thcse infants were treated because their mothers had positive serologic reactions, or thcir tests were negative but they had a history of syphilis and had received no antisyphilitic treatment during pregnancy. The initial dose of 0.0625 gm. was soon increased to 0.125 gm. and the total dosage given was 8.0 gm. Of the entire number only 3 premature infants died in thc first few days of life, the others being dismissed with proper weights. Only 28 of these children were followed for 1 year—22 were negative at birth and the others became negative with treatment.

James (*87*) reported good results in the treatment of 9 cases of ocular syphilis, including 6 of interstitial keratitis, in patients varying in age from 15 to 33 years. The dose of stovarsol was 0.25 gm. 3 times a day; intramuscular injections of mercury in addition to stovarsol were given to 6 patients. The total dosage of stovarsol varied between 49.5 and 100 gm. The Wassermann reaction which had been strongly positive in 8 patients at the beginning of treatment reversed to negative in 5 after from 9 to 32 weeks of treatment.

The only study on the intravenous use of acetarsone in congenital syphilis is that of Givan and Villa (*71, 72*) who treated a total of 43 children varying in age from 2½ to 14 years. Thc injections were given at weekly intcrvals in dosages ranging from 0.2 to 1.0 gm. No local or systemic reactions were observcd. The only untoward reaction observcd was nausea and vomiting which occurred in 1 child after the sixth injection. These authors reported that in interstitial keratitis intravenous acetarsone had no advantage over neoarsphenamine. In regard to the Wassermann reaction they found that 16 (37 percent) paticnts had a reversal of the Wassermann reaction following treatment; 13 (30 percent) remaincd Wassermann positive, and in 14 (33 percent) the reaction was modified. However, many of the patients treatcd had received one or more courses of treatment with neoarsphenamine and heavy metal, mostly bismuth, before treatment with acetarsone was givcn, and their Wassermann reactions were only slightly positive before acetarsone treatment. In their earlier report the authors stated that the total number of injections given to 30 children was 463; in the later report the total dosage is not given.

Summary of Acetarsone Treatment Results in Congenital Syphilis

In regard to the effect of acetarsone on the clinical manifestations, the response was good and there was no cssential difference in the results obtained with different dosage schemes. Skin lesions healed in an average period of 2 to 3 weeks; the same was true of Parrot's pseudoparalysis. Syphilitic bone lesions healed in the great majority of cases, as evidenced by roentgen-ray examination. A longer period of treatment was required to cure snuffles, the average period being 4 to 8 weeks. Splenomegaly

and hepatomegaly persisted beyond the period of observation in many cases, in others it disappeared in from 6 weeks to 6 months. The results in interstitial keratitis were, on the whole, poor. In one of Lyon and Seymour's cases interstitial keratitis developed after the child had been receiving acetarsone for 1 week.

In regard to serologic reversal, the only results reported with the low-intermittent dosage scheme are those of Oppenheim and Fessler who treated 11 infants and 23 children (15 aged 3 to 13 years and 8 aged 16 to 26 years), obtaining 8 percent and 11 percent of reversals, respectively, and those of Scherber who observed practically no change in the serologic reactions of 9 infants and 13 children. Although the number treated is too small for definite evaluation, the results seem to indicate that this type of dosage is not high or intensive enough to be effective.

In table 2 the effects of low-continuous and high-continuous therapy in regard to serologic reversal, as reported by various authors, are summarized, the results obtained in infants being shown separately from those obtained in children. Infants in the first weeks of life who were treated prophylactically (no serologic test taken, or negative serologic findings but a syphilitic mother) or on the basis of a positive serologic test alone (reaginemia) are not included because it is impossible to say how many of these infants were actually infected with syphilis, and therefore the results of their treatment cannot be evaluated.

This table shows that the effect of low-continuous and high-continuous treatment on serologic reversal, both in infants and children, is practically the same and that serologic reversal occurs only half as frequently in children as in infants. As a rule the younger the child when treatment was started, the better the chance of serologic reversal. In a total series of 376 infants treated by these dosage schemes serologic reversal was obtained in 69 percent, and in the total series of 330 children so treated 34 percent reversals were obtained.

A number of authors did not separate the percentages of serologic reversal obtained in infants from those obtained in children. Rosenbaum obtained 50 percent of reversals in a group of 395 children of all ages; Korman, Smith and Abt 43 percent in a group of 98 children (70 infants and 28 children, who also received bismuth); von den Steinen 89 percent in a group of 9 children (6 infants and 3 children some of whom also received bismuth); Hom 27 percent in a group of 46 children; Kundratitz 80 percent in a group of 15 children (the last 3 authors used the high-intermittent dosage scheme). These authors also did not report definitely on the length of the observation period following serologic reversal. In this total group of 628 children of all ages serologic reversal occurred in 45 percent.

TABLE 2.—*Incidence of serologic reversal in infants and children with acetarsone therapy*

Infants under 2 years [1]			Children		
Number treated	Percent reversal	Observation period	Number treated	Percent reversal	Observation period
A. Low—Continuous Dosage Scheme					
16	37. 5	Not stated.	44	34. 1	Not stated.
21	80. 6	Do.	8	37. 5	Do.
4	75. 0	Two, 6–9 months.	9	50. 0	Do.
5	40. 0	Not stated.	10	20. 0	Do.
22	72. 7	1 year.	26	34. 6	Do.
4	100. 0	Not stated.	10	50. 0	Do.
5	100. 0	Do.			
[2] 8	75. 0	Do.			
23	82. 6	Do.			
108	73. 7		107	37. 7	
B. High—Continuous Dosage Scheme					
9	89. 0	Not stated.	9	22. 0	Not stated.
26	34. 6	Do.	105	36. 0	1–3 years.
21	33. 0	Do.	46	20. 0	Not stated.
[3] 30	97. 0	Up to 2½ years.	25	40. 0	Do.
30	70. 0	1–3 years.	38	34. 0	10 patients 1–3 years.
27	74. 0	Not stated.			
25	40. 0	Do.			
15	67. 0	Do.			
24	80. 0	Do.			
61	68. 0	Do.			
268	65. 2		223	30. 4	

[1] The majority under 1 year of age.
[2] Received bismuth also.
[3] Hospitalized during entire treatment period.

NOTE.—Nabarro's results not included because many of the children received other therapy, i. e., sulfarsphenamine, acetylarsan.

Müller who treated only children under 2 years of age with his very high-dosage intermittent scheme strongly advocated the prophylactic treatment of all infants whose mothers had been inadequately treated during pregnancy. In his published reports he does not indicate how many of these infants were definitely syphilitic, and for that reason his results (95 to 100 percent negative serologic reactions following treatment) cannot be evaluated. The same is true of Meyer's and also of Eckhardt's reports.

So few of the children treated were kept under observation that it is impossible to determine from the reports whether the treatment results were permanent or how many of the children had serologic or clinical relapse. That serologic relapse does occur is shown by isolated reports. In 3 of the 16 infants treated by Danzer the serologic reaction became negative following treatment but later was found to be strongly positive. In 1 of Klaften's infants treated prophylactically, a syphilitic skin eruption and a positive Wassermann reaction developed during the course of treatment and did not respond to continued spirocid treatment but later responded to arsphenamine. In 2 infants treated by Müller serologic relapse occurred after 1 and 2 years respectively. According to Kundratitz serologic relapse was more frequent following spirocid than following neoarsphenamine therapy. Nabarro who, on the average, observed the majority of children treated by him for a longer period of time than most investigators, namely, for periods varying from several months to 5½ years, noted the occurrence of serologic relapse in 2 out of 43 children. In 1 child whose treatment was started at 1 year of age the Wassermann reaction had become negative at the age of 16 months (after 1.2 gm. sulfarsphenamine and 29 gm. stovarsol) and had then relapsed to positive at the age of 5 years. In another child whose treatment was started when she was 5½ years old, the blood Wassermann reaction became negative 2 years later (following stovarsol, bismuth, and mercury) but was again strongly positive after another 1¼ years. Nabarro obtained good results in the group of 43 children treated chiefly with stovarsol, serologic reversal occurring in 27 (84 percent) of a group of 32. A number of these children however received other drugs in addition to stovarsol, e. g., acetylarsan, sulfarsphenamine, and large amounts of bismuth and mercury.

On the basis of these clinical and serologic results the Bratusch-Marrain low-continuous dosage scheme which causes fewer toxic reactions than higher dosage yet produces equally good results is the treatment method of choice.

Toxic Reactions Observed in the Acetarsone Treatment of Congenital Syphilis

With the low dosage–intermittent scheme of acetarsone therapy, Oppenheim (*155*, *156*) apparently observed no serious toxic reactions since none are mentioned in his reports. Scherber (*177*) found it necessary to discontinue treatment in one child because a toxic exanthem developed.

Of the authors using the low dosage–continuous scheme Juarros and Galarreta (*91*), Danzer (*42*) and Bratusch-Marrain (*20*) reported that they had observed no serious untoward reactions. In a group of 65 children treated by Abt and Traisman (*1*) and by Traisman (*205*, *206*) they noted pathologic urinary findings such as albumin, casts, and erythrocytes in the

majority of them at one time or another during treatment. Diarrhea occurred in two infants. In five children an arsenical skin eruption was observed. There was one fatality. This occurred in a 6-year-old Negro girl. After she had received a total of 6.5 gm. of stovarsol in 4 weeks, albumin, erythrocytes, and granular casts were found in the urine. Administration of the drug was discontinued, but a scaly eruption of the chest and abdomen appeared which was followed 4 days later by diarrhea, abdominal pain, and a temperature of 100° F. She died on the seventeenth day. Autopsy was not permitted.

Rosenbaum and Faulkner (*174*) reported 5 deaths in a series of 395 children treated. A 5-month-old boy contracted pertussis in the fifth week of acetarsone treatment and died of bronchopneumonia; a 4-month-old boy with bilateral otitis media in addition to syphilis was given 0.06 gm. acetarsone daily for 3 days and died of bronchopneumonia after 3 days of treatment; a 3-month-old boy was given 0.06 gm. of acetarsone daily for 3 days at which time the drug was discontinued because the child seemed very ill—he died 3 days later; a 6-week-old girl died after 0.06 gm. of acetarsone had been given over a period of 2 days. The fifth death occurred in a girl 8 years of age. She had been treated with acetarsone over a period of 3 years. Her erythrocyte count and the hemoglobin content of the blood had always been low, and she had been almost continuously treated for anemia. She died with the blood and clinical picture of aplastic anemia. The other toxic reactions observed by them were not fatal. A 6-month-old boy had a temperature of 104° F. and convulsions after he had received 0.06 gm. for 2 days. He was transferred to a private physician who continued his treatment. A 9-month-old girl had a temperature of 104° F. on the day after treatment with 0.06 gm. acetarsone. The administration of the drug was stopped; when it was again tried later, fever again developed. In 7 children erythematous skin eruptions developed (6 of these were able to tolerate acetarsone after a rest period). All of these reactions occurred a few days after treatment had been started except in 1 child in whom the reaction occurred after 3 weeks of treatment and who was not able to tolerate the drug thereafter. In 1 child a generalized macular eruption appeared 12 days after treatment had been started and a 6-year-old girl had severe exfoliative dermatitis following 1 course of treatment.

Among 32 infants treated by Rambar (*168*) 3 had diarrhea as a result of treatment. In each case this occurred during the fifth or sixth week of therapy after a total dosage of from 2.5 to 3 gm. In 2 infants an urticarial eruption developed on the extremities and in another infant a diffuse redness of the skin on the face, trunk, and extremities which was followed by generalized desquamation. In 11 out of 20 infants whose urine was examined, a trace of albumin was present at some time during treatment.

Yampolsky (*223*) reported that fever and edema occurred in some cases; he noted transient pyuria in 1 child and a scaly skin eruption of the face in another child. Among 20 children treated by Coppolino (*38*) vomiting occurred in 1 child and erythema of the buttocks in 2 children. In 1 of the 5 children treated by Friedman (*66*) vomiting, diarrhea, and a morbilliform skin eruption developed after a total dosage of 3.42 gm. Fan (*55*) stated that diarrhea was the chief untoward reaction which he encountered. Among the 32 children treated by Arena and Gay (*5*) vomiting and diarrhea occurred in 4, arsenical dermatitis in 2, and mild hemorrhagic nephritis in 1 of the children. Among the 29 patients treated by Paddle (*160*) (mental defectives of all ages) toxic reactions, chiefly skin eruptions, occurred in 13. One of his patients, who was 61 years of age, died of aplastic anemia which occurred suddenly at the end of the 5th course. In Korman, Smith and Abt's (*101*) series of 98 children gastrointestinal disturbances occurred in 13 (usually diarrhea) and skin eruptions in 5. Albuminuria occurred in some of the children, in 1 this was associated with casts and erythrocytes in the urine.

Nabarro (*142*), who used stovarsol in the treatment of 117 children, reported the occurrence of 14 (34 percent) toxic reactions among 41 infants in this group and 11 (14.4 percent) toxic reactions among 76 older children. These reactions were mild as a rule and consisted of diarrhea, skin eruptions, vomiting, fever, and abdominal pain. In 3 of the infants the diarrhea and vomiting which developed on stovarsol therapy resulted in death. One instance of paresthesia was noted in an older child.

High dosage–intermittent scheme.—Among 6 infants on whose treatment Klaften (*95*) reported in 1927, toxic exanthemata developed in 2 and fever in 3 as result of treatment. In 1928 (*96*) he reported that Herxheimer reactions in the form of fever and scarlatiniform exanthemata occurred frequently during treatment with spirocid. Of the 61 infants treated by Baumbach (*11*) 18 (29.5 percent) died, but only 1 of these deaths was considered to have been caused by spirocid treatment; it occurred after 2 weeks of therapy. Out of 80 children treated by Hom (*82*) 14 died, but spirocid treatment was considered to have been responsible for only 1 of these deaths which occurred on the twelfth day of treatment and after a total dosage of 0.7 gm. Many of the children had gastrointestinal disturbances as a result of treatment. A Herxheimer reaction characterized by elevation of temperature after the first dose of the drug was a very frequent finding; in 1 case spirocid administration resulted in continuous elevation of temperature. Exanthemata occurred in 5 children, appearing at the end of the first day, on the fourth day, and at the end of 2 weeks of treatment (2) respectively. These eruptions were macular or maculopapular and were sometimes associated with edema.

Of a total of 38 infants whom Müller (*138*) personally studied and treated with spirocid 3 died before treatment was given; 5 (14 percent) died during or after treatment. Apparently Müller did not attribute any of these deaths to the action of the drug; he did not even mention any specific instances of intolerance observed in the children he treated. He merely said that fever, exanthemata, and diarrhea do not as a rule necessitate interruption of treatment. However, Martin (*124*) reported 2 cases of paralysis, 1 flaccid and 1 spastic in type, which occurred in infants as the result of spirocid treatment according to the Müller dosage scheme. Both infants were seronegative and were treated prophylactically. Treatment with spirocid was started in the first infant 3 days after birth. Flaccid paralysis of both arms and legs was noted after 16.5 gm. of the drug had been given. This child had shown no symptoms of intolerance. The paralysis apparently was permanent since the child had to be institutionalized at the age of 3 months. In the second infant spirocid treatment was started 16 days after birth. The dosage was gradually increased in spite of the fact that the infant vomited. After a total of 16.9 gm. flaccid paralysis developed. This condition improved when the drug was stopped, but afterwards it was again administered; a total of 24 gm. was given. At the age of 2½ months the infant was admitted to the children's hospital with spastic paralysis of the legs. Because of this experience the author advised that the total dosage for the first course should not exceed 9 or 10 gm. in the newborn.

Meyer (*132*), who also used the Müller dosage scheme, observed 1 case of spastic paralysis of the extremities with nystagmus and hoarseness which occurred in the sixth week of treatment. In 1933 Müller advised against the use of spirocid in older children, saying that death due to encephalitic punctata had been observed as result of spirocid therapy.

Cibils Aguirre and de las Carreras (*34*) treated 96 children with paroxil, using the Müller dosage scheme. (Only 5.7 percent of these children had manifestations of syphilis, the others were treated because their parents were probably or definitely syphilitic.) Untoward reactions occurred in 23 (24 percent) and included vertigo (1), tachypnea (2), vomiting (4), diarrhea (8), fever (4), generalized dermatitis (2), and flaccid paralysis of the legs (2). The flaccid paralyses occurred with dosages of 7.5 and 14 gm. of paroxil in children of 11 and 15 years of age, respectively, and 1 case of generalized dermatitis with 26 gm. In all except 4 of these cases of intolerance (including the paralyses), the drug could be resumed after a rest period.

Bernheim-Karrer (*14*) reported a case of spastic tetraplegia due to spirocid which occurred in an infant on treatment according to the Müller dosage scheme. This infant had been given spirocid prophylactically. At the end of the third month, after a dosage of 26.75 gm., nystagmus with flaccid

tetraplegia developed which later became spastic. This child remained mentally markedly retarded and died at 2½ years with epileptiform seizures. At autopsy leptomeningitis, external hydrocephalus, and asymmetry of the brain were found. The pathologist ruled out syphilis as having produced these changes and attributed them to arsenic.

Among 16 infants treated by Huber (*83*) 2 died of intercurrent infection during treatment. In 13 of the infants the urine was found to be normal while 3 had albuminuria (present in 1 before treatment); 3 had transitory diarrhea, 1 had fever on the second day of treatment, and 1 had fever and a morbilliform skin eruption on the second day of treatment. Six out of seven older children treated had Herxheimer reactions (fever of 39° C. and exanthem). Malaise and headache occurred in 2 children.

In a certain number of cases Eckhardt (*48*) observed fever (temperature of 38°–41° C.) following the first dose of spirocid or following an increase in the dosage. A Herxheimer reaction occurred in 1 infant and exanthemata in 2 infants. One infant died; it had been receiving only 0.062 gm. daily but the administration of the drug was continued in spite of diarrhea.

Nedelmann (*143*) who used the Müller dosage scheme reported 1 death from pyuria which occurred in an infant under spirocid treatment. A Herxheimer reaction occurred in the majority of infants treated, characterized by fever following the first dose of the drug. A transitory exanthem occurred in 1 infant, and although diarrhea was a symptom noted, it was not severe enough to cause the author to discontinue treatment.

High dosage–continuous scheme.—Krombach (*107*) reported 2 deaths among the children she treated with spirocid. One of these children died of bronchopneumonia after 3 weeks of drug treatment, and the other died of an infection 8 weeks after treatment was started. Herxheimer reactions were observed in 3 cases, a mild toxic exanthem in 1 case, and diarrhea in a few.

Soldin and Lesser (*193*) observed a condition in infants which was similar to but not quite so severe as collapse when the initial dose of spirocid was not extremely small. A similar condition in older children was characterized by pallor and slightly subnormal temperature.

Courtin (*39*) reported the case of a 2-month-old infant in whom after 18 days of treatment according to the Tuscherer scheme a generalized macular skin eruption developed which was associated with albumin, hyaline casts, and erythrocytes in the urine (albumin had been present since treatment was started). In spite of these findings a rest period of only 4 days was allowed and the drug again given in reduced dosage. The eruption then became urticarial-bullous in type and was associated with edema of the hands and feet. The infant died 6 days after the appearance of the rash. At autopsy diffuse interstitial hepatitis and bronchopneumonia were found. Another infant 3½ months of age had a fever of 39.6° C. and a macular

exanthem on the ninth day of treatment together with slight albuminuria. The drug was discontinued following which there was gradual recovery. He advised that the drug be discontinued at the slightest sign of intolerance.

Herz (*78*) reported the case of a 9-month-old nonsyphilitic infant (abscess in the groin) in which symptoms comparable to those of arsphenamine encephalitis, with vomiting, fever, and exanthem, developed following a total dosage of 0.6 gm. (daily dose 0.062 gm.). On withdrawal of spirocid there was gradual recovery.

Opitz (*147*) reported on 3 children ages 5 to 13 years who had generalized lymphogranulomatosis and in whom, following 8 to 11 days of administration of spirocid (Tuscherer scheme) severe cerebral manifestations developed which ended fatally in 2 cases. The third child was taken home by its parents and recovered. Autopsy in 1 child showed the typical picture of cerebral purpura such as occurs in arsphenamine intoxication.

The toxic reactions reported by Menne (*129*) in the series of 18 infants treated by her (highly variable dosage) were diarrhea (9), vomiting (1), restlessness (2), mild urticarial exanthem (2), and petechia of the skin (2). During spirocid treatment 4 infants died—2 of severe visceral syphilis, 1 of bronchopneumonia, and 1 with acute proctitis. In the last infant, small areas of softening of the brain were found, which, according to the author, possibly were due to birth trauma. Mettenheim, who discussed this same series of cases, reported in addition icterus in 1 infant and collapse in 1 infant.

The untoward effects noted by v. Kiss (*93*) were vomiting (2 cases) and diarrhea (4 cases).

Schirlitz, Gierthmühlen, and also Hess, in the discussion of Jochims' (*89*) paper reported toxic reactions which they had observed. Schirlitz observed 2 cases of hematuria which disappeared when spirocid treatment was discontinued. Gierthmühlen found blood in the stools of 2 very young infants who were receiving 0.062 gm. of spirocid. This disappeared when the dose was reduced by one half. Hess observed an infant who developed arsenical neuritis after several weeks of treatment with spirocid.

Steinbach (*196*) reported the case of a 7-year-old congenitally syphilitic child in whom, following the administration of 17.25 gm. of spirocid within 35 days, a papular exanthem associated with fever, headache, and conjunctivitis developed. In spite of the fact that the administration of the drug was stopped, the eruption became bullous-pustular in type associated with vesicles of the mucosa of the mouth. A fever of 40.1° C. lasted for 10 days. The exanthem began to fade on the seventh day and was completely gone by the twenty-seventh day. The eosinophilia in this case was remarkable. The values increased from 12.5 percent on the third day to 31 percent on the eighth day at which time the leukocyte count was 40,600.

Among the infants treated by Maxwell and Glaser (*126*, *73*) flaccid paralysis developed in 2 of them who were less than 1 month of age when treatment was started. The paralysis developed on the thirty-third and thirty-first days of treatment respectively and after 7.5 and 7.68 gm. of the drug had been given. One infant recovered slowly, whether completely or not is not stated; the other infant died. In a later report on these 2 cases Glaser stated that he believed that acute arsenical myelitis had developed, with resulting or accompanying arsenical neuritis and paralysis. The spinal cord of the infant which had died was sectioned at various levels. On the basis of a study of these sections a diagnosis of myelitis was made. Among children over 1 year of age who were treated with acetarsone 1 had, as the result of treatment, a morbilliform rash, conjunctivitis, malaise, apathy, and albuminuria. Four children had transient albuminuria, 1 had a few erythrocytes in the urine, and 1 had hyaline casts.

Of the 196 patients in Pillsbury and Perlman's (*162*) series who received some acetarsone, 21 (10.7 percent) had some type of toxic reaction. These included nephritis (8), gastrointestinal disturbances (7), mild dermatitis (3), gastrointestinal disturbances and dermatitis (1), fixed eruption (1), severe peripheral neuritis, hepatitis, and dermatitis (1). Acetarsone therapy had to be permanently discontinued in 10 patients because of toxic reactions. The last case was the most severe toxic reaction observed. It occurred in a 1-year-old Negro girl. A generalized dermatitis with a temperature of 104° F. developed after 4 weeks of treatment. She was admitted to the hospital where marked enlargement of the liver, paralysis of the left external rectus muscle, absence of knee and ankle reflexes, and bilateral foot and wrist drop developed. Definite improvement occurred within 2 weeks. An interesting finding was that among 22 children who were being treated with acetarsone in the hospital, 7 (31.8 percent) had toxic reactions whereas of 174 children receiving treatment at home only 14 (8 percent) had these reactions. The only adequate explanation the authors could find for this was that the patients who were being treated at home were not receiving the drug as prescribed. One death occurred in a premature infant 1 month after acetarsone had been discontinued because of acute hemorrhagic nephritis which cleared up in 1 week. The patient was removed from the hospital against advice. The authors stated that they believed this death was not caused by acetarsone.

Smith and Lyon (*190*) reported the case of a 7-year-old girl with congenital syphilis in whom a severe form of aplastic anemia developed suddenly, apparently due to the arsenicals used in treatment. The antisyphilitic treatment had extended over a period of 10 months and had consisted of 10 injections of a bismuth preparation, 6 injections of 0.1 gm. neoarsphenamine, and 4 courses of stovarsol (total of 56 gm.), administered

according to the Maxwell-Glaser scheme. Following 11 blood transfusions the child gradually recovered.

The only toxic effects noted by Davidson and Birt (*44*) were headache in 2 children and a combination of coryza and gastrointestinal disturbance in another child.

Van Dermark (*46*) noted that vomiting and diarrhea occurred most often in young infants (4 and 9 infants, respectively), and albuminuria occurred most often in older children (5 children).

Mahler (*122*) reported the occurrence of paralysis of the lower extremities in 4 infants treated by her according to the Tuscherer scheme; 2 of these infants died. Because of this experience she advised that if spirocid has to be used at all, it should be given in smaller doses with frequent rest periods of several days to permit excretion of part of the arsenic.

Soto Pradera (*194*) reported the case of a 6-month-old infant with congenital syphilis who was treated with stovarsol according to the method of Maxwell and Glaser. After 5 weeks of treatment severe diarrhea developed and a few days later a papulovesicular eruption. The drug was discontinued. Three days later flaccid paralysis of the extremities and icterus developed. The icterus disappeared in 6 weeks, the paralysis after 6 months of physiotherapy. Diarrhea occurred in 2 other infants treated and was associated in one of these with icterus and in the other with irritability.

Lyon and Seymour (*121*) observed untoward effects in 13 infants, consisting of diarrhea (8), vomiting (5), stomatitis (2), skin eruption (1), and intermittent albuminuria (1). In the older children, as reported by Lyon and O'Neil (*120*) albuminuria occurred in 6, and arsenical dermatitis, abdominal pain, and stomatitis each occurred once.

Without mentioning the dosage used, Signorelli (*188*) reported that he had observed 2 newborn syphilitic infants in whom the administration of stovarsol apparently precipitated the onset of renal lesions which eventually led to death. Gerth (*69*) reported the case of a 3½-month-old infant with severe skin and visceral syphilis who after having received 0.125 gm. spirocid in 2 days had a severe Herxheimer reaction. Treatment was discontinued for 7 days. Following this he received in a period of 10 days a total of 0.115 gm. spirocid. At this time the drug had to be discontinued again because of diarrhea. A "toxic dyspepsia" developed which resulted in death. At this time and at autopsy no signs of syphilis could be found.

TABLE 3.—*Toxic reactions produced by acetarsone in children*

Treatment scheme	Number of authors reporting reactions	Number of patients with reactions reported	Moderate reactions	Number	Severe reactions	Number	Deaths	Number
Low-intermittent.	1	1	Exanthem	1				
Low-continuous.	11	117	Exanthemata	50	Convulsions	1	Other, less definite causes.	4
			Diarrhea	28				
			Vomiting	11			Diarrhea and vomiting (infants).	3
			Albuminuria	11				
			Nephritis [1]	2				
			Fever (continuous).	2			Aplastic anemia.	2
			Paresthesias	1			Exfoliative dermatitis.	1
			Pyuria	1				
High-intermittent.	11	64	Exanthemata	13	Paralysis	5	Other, less definite causes.	9
			Diarrhea	11				
			Fever	9				
			Vomiting	4			Flaccid tetraplegia.	1
			Alhuminuria	3				
			Headache	2			Diarrhea	1
			Malaise	2			Pyuria	1
			Tachypnea	2				
			Vertigo	1				
			Herxheimer [2] (fever-exanthem).					
High-continuous.	19	133	Diarrhea	40	Nephritis	11	Other, less definite causes.	6
			Alhuminuria	17	Paralysis	3		
			Vomiting	13	Arsenic encephalitis.	2	Paralysis	2
			Exanthemata	9				
			Herxheimer	3	Skin petechiae	2	Encephalitis	2
			Stomatitis	3	Icterus	2	Bullous exanthem.	1
			Restlessness	3	Bullous exanthem.	1		
			Headache	2				
			Blood in feces	2	Arsenic neuritis.	1	Acute arsenical myelitis.	1
			Conjunctivitis	1				
			Fixed eruption	1	Aplastic anemia	1	Nephritis	1
			Malaise	1	Severe hepatitis	1		
			Collapse [3]		Severe dermatitis.			
					Peripheral neuritis.			
					Diarrhea	1		
					Icterus			
					Flaccid paralysis.			

[1] Traisman and others reported finding of albumin, erythrocytes and casts in urine of many children under treatment. Definite number not stated.

[2] Noted by many authors including Eckhardt, Hom, Klaften, Huber, Nedelmann, in large number of children.

[3] A certain number of infants—Soldin and Lesser, and Mettenheim.

Summary of toxic reactions.—It can be said in general (table 3) that the low intermittent dosage scheme of acetarsone administration results in fewer toxic reactions than the more intensive treatment schemes. Whether this low dosage is at the same time therapeutically effective, is an important consideration. Many authors were of the opinion that the Oppenheim dosage scheme is not therapeutically effective and therefore did not use it or, after having tried it, discarded it as ineffective. Since Oppenheim administered bismuth concomitantly, it is difficult to evaluate his acetarsone treatment results, especially since they have not been reported in sufficient detail. The more treatment is intensified, as shown by a comparison of low-continuous, high-intermittent, and high-continuous dosage, the more numerous and more severe do the toxic reactions become. On the basis of a study of the literature it can be definitely concluded that the Müller dosage scheme should be discarded since 7 of the 12 deaths as well as all 5 cases of flaccid or spastic paralysis, observed in the group receiving high-intermittent therapy, occurred with the Müller dosage scheme. Müller himself warned against using spirocid in older children because he had observed encephalitis in them as the result of his treatment.

Of the high-continuous schemes of dosage both the Tuscherer and the Maxwell-Glaser schemes have produced severe toxic reactions, the former more than the latter, as would be expected since it is a more intensive scheme. Of the deaths reported, 5 (1 bullous exanthem, 2 encephalitis, 2 paralysis of the lower extremities) occurred following the Tuscherer dosage and, 2 (1 nephritis, 1 arsenic myelitis) following the Maxwell-Glaser dosage. Of the severe reactions with final recovery of the patient, 3 (1 encephalitis, 2 paralyses of the lower extremities) occurred with the Tuscherer, and 3 (2 flaccid paralyses, 1 aplastic anemia) with the Maxwell-Glaser dosages.

Unfortunately the percentage incidence of toxic reactions for all the authors cannot be calculated, because many of them made only general statements regarding toxic reactions, and others (particularly those who used high toxic doses and observed severe reactions) reported only the serious reactions such as paralysis, convulsions, exfoliative dermatitis, with no mention made of less serious reactions. In table 4 are shown the number and percentage of toxic reactions based on the reports of those authors who gave sufficient data from which to obtain this information.

TABLE 4.—*Incidence of toxic reactions due to acetarsone in children* [1]

Author	Number of patients treated	Number of toxic reactions	Percent of toxic reactions
Bratusch-Marrain dosage scheme			
Traisman	65	8	12.0
Rosenbaum and Faulkner	395	16	4.0
Rambar	32	6	18.8
Coppolino	20	3	15.0
Friedman	5	1	20.0
Arena and Gay	32	7	22.0
Paddle	29	13	44.8
Korman, Smith, and Abt	98	19	19.4
Nabarro	[2] 41	14	34.0
	[3] 76	11	14.4
Total	793	98	20.0
Higher dosage			
Cibils Aguirre and de las Carreras	96	23	24.0
Huber	23	11	48.0
Pillsbury and Perlman	174	14	8.0
Do	[4] 22	7	31.8
Total	315	55	28.0

[1] This series includes only a few of the serious reactions that were reported. Other authors gave incomplete data.

[2] Institutionalized infants.

[3] Institutionalized children.

[4] Children treated in hospital.

It will be seen that among 793 children treated by 9 authors according to the Bratusch-Marrain low-dosage scheme 98 (20 percent) had toxic reactions, and among 315 children treated by 3 authors according to higher dosage schemes 55 (28 percent) had toxic reactions. These figures do not include abnormal urinary findings observed in a large number of children.

Among Nabarro's institutionalized children, in whom the administration of the drug could be controlled, the incidence of toxic reactions was 34 percent among infants and 14.4 percent among older children. Pillsbury and Perlman found an incidence of 31.8 percent of toxic reactions among hospitalized children as compared to 8 percent among children treated at home.

A survey of toxic reactions per se, without regard to therapeutically effective dosage, leads to the conclusion that acetarsone is a definitely toxic drug, regardless of dosage; that in general its toxicity increases in direct

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proportion to the dosage and that the best way to protect the patient against its toxic effect is to give him as little acetarsone as possible. A safer drug is to be preferred even if its administration is more difficult.

The toxic reactions observed in adults in relation to dosage and types of reaction produced are essentially the same as those observed in children.

On the basis of reports in the literature, acetarsone should not be given in the presence of intercurrent infections, since these apparently increase its toxic action.

DISCUSSION

Most observers are agreed that acetarsone has antisyphilitic action. Workers in the experimental field and syphilologists, who because of their wide experience with the arsphenamines are qualified to make a comparison, have found the antisyphilitic action of acetarsone to be considerably inferior to that of arsphenamine. Some of them have found its action to be about the same as that of bismuth while others consider its action inferior to that of bismuth and compare it to that of mercury (*37*, *162*, *163*).

The only apparent reason for the use of acetarsone in the treatment of congenital syphilis is the fact that it can be given by mouth. But this great advantage from the technical point of view is actually a great disadvantage. The experience of Pillsbury and Perlman, as well as that of Jochims and probably also of Yampolsky in his series of Negro children, has shown that the parents either do not give the prescribed drug to the child to be treated, or they give it irregularly. The fact that the incidence of toxic reactions among hospitalized patients was 4 times greater than that observed among out-patients in Pillsbury and Perlman's series, and that among Yampolsky's Negro children neither toxic reactions nor the usual therapeutic response occurred, supports this assumption. Jochims, who treated a large series of hospitalized children with acetarsone, reported that he had found ambulant treatment with acetarsone to be unsuccessful because the parents did not feed the tablets regularly to the children, and it was impossible for him to control its administration. This factor alone places acetarsone in a secondary position in the treatment of congenital syphilis, unless it is possible to institutionalize the children for the entire duration of treatment and that, of course, is practically impossible.

Eliminating the discomfort and inconvenience of intravenous therapy by prescribing acetarsone also does not necessarily increase clinic attendance. Pillsbury and Perlman found clinic attendance to be exactly the same on peroral as on intravenous methods of treatment. Korman, Smith and Abt also reported that the use of acetarsone did not result in better clinic attendance.

The results of experimental studies of acetarsone in animals show marked variations in toxicity as determined by different investigators and also

among the animals of any single investigator. The same variable and unpredictable results were obtained in the prophylactic and curative treatment of animals which had been experimentally infected with syphilis. Acetarsone in dosage equivalent to the prophylactic and therapeutic doses usually employed in human syphilis was found to be ineffective. Kemp, in an editorial (*49*) pointed out that one of two hypotheses must be assumed to account for these divergent findings: First, there may be such wide variation in the toxicity of various preparations of the drug that it is impossible to determine its toxic dose for rabbits; or second, there may be a wide range of individual susceptibility in rabbits unlike that shown to most other drugs. In either event, according to Kemp, proposals for its use in the treatment of human syphilis have been made without sufficient regard for its toxicity for experimental animals; these variations in toxicity also have made it impossible to provide convincing evidence of therapeutic efficacy in rabbit syphilis.

According to the findings of Worms (*218*), the effect of acetarsone in experimental animals is one of insidious poisoning. He therefore cautioned that it be used with great care in human beings. In a number of reports of deaths which occurred among infants on acetarsone therapy, the cause of death was obscure. In these, death may have been due to this insidious action of acetarsone.

The results obtained by the majority of investigators in the prophylaxis of syphilis and the treatment of early acquired syphilis have conclusively shown that the effect of acetarsone is definitely inferior to that of arsphenamine. With acetarsone therapy the spirochetes disappear less promptly and less regularly from the lesions, the lesions heal less rapidly, the effect on serologic reversal is less marked, and treatment failure is more common.

That acetarsone is a highly toxic drug is apparent from the number and severity of toxic reactions which have been reported both in adults and children. The incidence of toxic reactions among adults was found to vary from 7 percent on the lowest (effective?) dosage to 30 percent on higher dosage. Among children, 20 percent of toxic reactions (34 percent among institutionalized infants) were observed with the most careful effective dosage scheme, namely that of Bratusch-Marrain. The fact that a very small dose not infrequently produces a serious toxic reaction makes its use still more hazardous.

In evaluating the results obtained in the treatment of congenital syphilis in infants and older children, a number of factors must be taken into consideration.

Even those pediatricians who consider acetarsone to be the "ideal" drug for the treatment of congenital syphilis in infants, do not find this drug very effective in the treatment of children over 2 years of age. For that reason some of them have combined acetarsone treatment with bismuth

or mercury therapy, whereas others have rejected acetarsone for the treatment of children and use neoarsphenamine and bismuth (*138, 204, 206*).

It is well known that the earlier in infancy the treatment of congenital syphilis is started, the better the chance of cure. Among others, E. Hoffmann (*81*) and also Ingraham and coworkers (*84*) have pointed out that there is a tendency toward spontaneous healing in less severe infections of congenital syphilis. An analysis of the outcome of the syphilitic infection was made by Ingraham and coworkers in 59 infants diagnosed as syphilitic. It was found that 13 were clinically and serologically cured with no treatment, 12 with inadequate treatment, and 15 with more than 1 year of active therapy; 10 had died who had received no treatment and 3 after inadequate treatment; 3 inadequately treated and 3 with more than 1 year's treatment still showed symptoms of syphilis. Spontaneous healing of bone lesions may occur. With bismuth therapy alone, Coppolino (*37*) obtained results in the treatment of infant congenital syphilis which were equally as good as those obtained with acetarsone therapy. (It should be added here that the occurrence of spontaneous healing in some cases of congenital syphilis never justifies withholding adequate treatment from any patient with congenital syphilis.)

In this connection it is also important to keep in mind certain obscurities in the diagnosis of infant congenital syphilis, because syphilis in the infant is sometimes diagnosed when it is not actually present. In the groups of infants whose treatment-results with acetarsone have been reported, there have been those whose treatment was begun too soon after birth to determine with certainty whether their positive serologic blood test was a definite indication of syphilitic infection or whether it merely indicated that some of the mother's reagin had passed into their blood and they themselves were not syphilitic (reaginemia). Most of the authors do not definitely clarify this point, many of them not even definitely separating infants with positive serologic reactions from those with negative serologic reactions (treated because the mother had syphilis). Cregor and Dalton (*41*) have pointed out that if all the infants with positive serologic reactions at birth were treated for syphilis 69 percent would be treated needlessly. Although most authors mentioned the effect of acetarsone on the manifestations of congenital syphilis, they did not indicate how many of the infants treated had manifestations and exactly what these manifestations were. It is well known that errors can be easily made in the diagnosis of bone syphilis in infants. Evans (*53*) has discussed in detail the roentgen-ray findings due to conditions other than syphilis upon which mistaken diagnoses of syphilis of the bone in infants have been made. As Whitridge (*214*) has demonstrated, bismuth lines from prenatal treatment also may be erroneously diagnosed as bone syphilis. Senear (*186*) has pointed out the

pitfalls in the diagnosis of syphilis in infancy in an excellent article on the diagnosis of syphilis in infancy and the teen age.

The observation period following the conclusions of treatment has not been sufficiently long in the great majority of infants and children treated with acetarsone to determine whether the effects of the drug were permanent. Whipple and Dunhan (*213*) have pointed this out in their interesting paper.

The following statements in regard to acetarsone have been made by outstanding syphilologists:

Stokes (*200*): "It will be apparent to those who have followed the discussions of the evaluation of syphilotherapeutic drugs thus far undertaken, that acetarsone has by no means proved its place in the treatment of syphilis, although a decade has elapsed since its introduction."

Moore (*136*): "Although the incidence of reactions in our smaller series of less closely observed patients is lower than in the Pillsbury and Perlman series, we agree with their conclusions that the effect of acetarsone in arresting congenital syphilis is inferior to that of other arsenical and bismuth preparations, and that its use is generally inadvisable, since it cannot be controlled by experimental studies of spirocheticidal action and toxicity in animals, and since administration to out-patients is not assured. In general, we feel that the same major objection applies to acetarsone as to any other oral method of treatment of syphilis: It is useful only in highly intelligent and highly cooperative patients; since many syphilitic patients do not qualify in these respects, its usefulness is sharply limited."

Cole (*35*) stated in 1936: "As yet I am unwilling to recommend the indiscriminate use of acetarsone by mouth in the treatment of congenital syphilis. It is still too much in the experimental stage."

Again Cole, in discussing Pillsbury and Perlman's (*162*) report stated: "It is well known how much the detail man emphasizes acetarsone for congenital syphilis. 'It is the drug of choice, particularly for infants,' 'You get better results in congenital syphilis with acetarsone than with any other preparation,' etc. Certainly Dr. Pillsbury did not find all those statements to be true. There is no question that acetarsone is effective against Spirochaeta pallida; it may be useful enough even to cure syphilis clinically. However, one must always remember that one is treating the patient as well as the syphilis, and when reactions occur in about 30 percent of cases, many of them very severe (nephritis in as many as 4 percent) one should certainly think twice before using that preparation further. I question whether there is a place in medicine today for acetarsone unless there is an enormous improvement in it. Too many remedies that may be used with comparative safety will give better results."

Dennie, also discussing Pillsbury and Perlman's report stated: "Any drug that causes as many reactions as this one [acetarsone] should be dis-

carded." Dennie and Pakula (*45*) stated that acetarsone cannot at this time be accepted as an effective antisyphilitic drug.

Pillsbury ended the discussion of his paper with the following statements: "It is certainly much more pleasant to run a clinic for congenital syphilis when treatment is given by mouth. We do not think, however, that our results justify its routine use."

E. Hoffmann (*87*) stated in 1938: "Recently the simplified method of treatment of employing spirocid (stovarsol) alone or in combined treatment has come to be regarded as sufficient. My best results were obtained with combined neoarsphenamine-bismuth treatment, of which 3 courses, separated by brief intervals, usually sufficed."

Kemp (*49*) pointed out that "sufficient time for long-term clinical evidence of 'cure' [in congenital syphilis], comparable with arsphenamine-bismuth data, has not as yet elapsed." He stated further: "Theoretically, the oral use of acetarsone in infantile congenital syphilis is to be deplored. This form of congenital syphilis is entirely analogous as to treatment response with acquired primary and secondary syphilis; i. e., it is curable, probably in the biologic sense of eradication of the last remaining treponeme as well as in the symptomatic sense of healing of lesions and prevention of relapse, and the serologic sense of permanent serologic negativity. This cure has been amply demonstrated to be capable of accomplishment with standard treatment methods, as in early acquired syphilis, with arsphenamine products and bismuth. However sympathetic one may be with the desire of parents and physicians to find a method of treating infants less painful and disagreeable than 'needles', the substitution of acetarsone for older proved methods offers a serious uncertainty of ultimate clinical outcome instead of a practical certainty; and that the use of the drug under these circumstances, and in view of its uncertainties in experimental animals, is hardly justified. It does not suffice for the proponents of acetarsone to offer evidence of healing of lesions or serologic reversal. Both of these phenomena may be accomplished by many treatment methods, specific, or nonspecific which are however, completely unsatisfactory for the chief aim of treatment of early syphilis, congenital or acquired, radical cure. Evidence that acetarsone will accomplish this is so far completely lacking. There are, it is believed, grounds for fearing that syphilitic infants treated orally with this drug may subsequently relapse, in high proportions, and unfortunately, such relapse may be irreparable.

"As matters stand at present, acetarsone by mouth has no proper place in the treatment of syphilis in human beings unless on a purely experimental basis. If such experimentation on man, without adequate previous evidence of the value of the drug in experimental animals, is justified at all, it should be limited to patients with late syphilis, congenital or ac-

quired, in whom radical cure is impossible, and in whom symptomatic relief and the prevention of relapse are the sole desiderata."

The following statements are taken from an editorial (*50*) appearing in the Journal of the American Medical Association in 1939: "Because of its inferiority of effectiveness, acetarsone cannot be recommended for general use in the treatment of syphilis. . . . In addition to the inferiority of results obtained in congenital syphilis with acetarsone, it has been found to be undesirable from the point of view of toxicity. . . . The small difference between the toxic and the therapeutic dose constitutes an additional objection to acetarsone."

The following is said about acetarsone in New and Nonofficial Remedies (*144*), 1941: "Acetarsone has been proposed for use both in prophylaxis and in treatment in certain cases of syphilis, but the evidence is thus far inconclusive."

Stokes and Ingraham (1939) (*201*): "There is, at the present time, no adequate substitute for injection therapy in appropriate dosage (in congenital syphilis). Acetarsone, while producing apparently good clinical results in some cases, in addition to being an untried drug so far as late accomplishment is concerned, must be considered relatively toxic if given in adequate dosage. The problem of regulating the dosage of an oral medication administered for a disease as serious as congenital syphilis by a mother with little or no training in the necessity for scientific accuracy will probably always remain an insurmountable difficulty."

At the present time, all the evidence on hand supports the stand taken by syphilologists. Unless the advocates of acetarsone therapy furnish proof based on well-controlled studies, their opinion that acetarsone is the "ideal" drug for the treatment of infantile congenital syphilis, still must be considered as opinion and not fact.

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MANAGEMENT OF CHANCROID

Granuloma Inguinale and Lymphogranuloma Venereum

IN GENERAL PRACTICE

ROBERT B. GREENBLATT, M. D.

FEDERAL SECURITY AGENCY
PAUL V. MCNUTT, *Administrator*

U. S. PUBLIC HEALTH SERVICE
THOMAS PARRAN, *Surgeon General*

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MANAGEMENT OF CHANCROID
Granuloma Inguinale and Lymphogranuloma Venereum in General Practice

Robert B. Greenblatt, M. D.

University of Georgia School of Medicine

Special Consultant to the United States Public Health Service

CHANCROID

Definition

Chancroid is an acute, localized, autoinoculable, genito-infectious disease characterized clinically by necrotizing ulcerations at the site of inoculation. The genital lesions are frequently accompanied by an inflammatory swelling and suppuration of the regional lymph nodes. In the medical literature the lesions are often referred to as ulcus molle, chancre mou, or soft chancre, and in the vernacular as soft sore (*72, 73*).

Etiology

For a long time, many investigators refused to ascribe a specific etiology to chancroid. This point is no longer open to dispute since Koch's postulates as to the causal organism have been repeatedly satisfied (*29*). The infectious agent is the *Hemophilus ducreyi*. It is a fine, short, Gram-negative bacillus with rounded ends. It is often referred to as a streptobacillus because of its tendency to group itself in chain formation, especially in cultures (fig. 1). In spreads from the lesion this characteristic morphology is but seldom present. The bacilli are found in small clusters, singly, or occasionally as parallel chains of two, three, or four organisms streaming along shredded strands of mucus. They are sometimes found in leukocytes. The *H. ducreyi* is a most fastidious organism but can be cultured (*26, 38, 64, 74*). Aside from the fact that it apparently requires some constituent in blood for its extracorporeal propagation, it has little in common with other members of the Hemophilus group.

Incubation Period

The incubation period is a very short one and generally is accepted as 3 to 5 days. However, if an abrasion is present at the time of contact, it is conceivable that a lesion may appear in 24 hours. On the other

hand, if the infectious agent is of low virulence, a delay in the appearance of the lesion may occur. These facts find corroboration in experimentally produced chancroid (*31*).

Epidemiology

The mode of infection is predominantly venereal except for accidentally acquired professional chancroid on the fingers of doctors, nurses, and orderlies. Prostitution is the most important source of chancroidal infection. It is a disease of the unenlightened and the common poor, of the dregs of society and of only the most indiscriminate of promiscuous men and women. At one time it was a disease met with frequently in seaports, cities, and towns on highways, but was rare in out-of-the-way towns and mountain villages. It followed in the path of traveling circuses, marathon dance teams and carnival shows, vagabonds of the road and their ilk. With the advent of the "trailer girl," the bawdy house on wheels, the itinerant whore, and the camp follower, it has become a disease of the byways as well. It is a disease of the unclean, of the people who do not use soap and water with any degree of frequency, particularly when coitus is performed on the run.

Some evidence has been presented which purports to show that there are carriers of the Ducrey bacillus just as there are carriers of typhoid and diphtheria (*3, 7, 63*). It may well be that some prostitutes remain carriers of the organism long after the chancroidal lesions have healed, and as such menace all who come in contact with them.

Incidence

Chancroid occurs endemically in the Mediterranean area, especially in Italy and Morocco, as well as in subtropical and tropical countries. It is certainly endemic in our Southeastern States. An analysis of the new admissions to the Cleveland City Hospital during 1937 yields the information that in this typical American city, 124 cases of chancroid were admitted in comparison to 92 of syphilis (*2*). During the same year in the typical southern city of Augusta, Ga., with one-fifteenth the population of Cleveland, 34 cases of chancroid were seen at the University Hospital Clinic along with 30 other cases in which chancroid complicated the picture of either syphilis, lymphogranuloma venereum, or granuloma inguinale.

An idea as to the incidence of chancroid may be gleaned from an analysis of the statistics of the United States Navy for the typical year 1929. The average strength of the Navy and Marine Corps for that year was 117,388. There were 3,652 cases (31.11 per 1,000 admissions) of chancroid in comparison to 2,540 (21.64 per 1,000 admissions) of syphilis (*8*).

In the British Army, Navy, and Air Force, the incidence of chancroid as compared to our own Army and Navy is about as common as syphilis, and its incidence is much higher among the forces stationed abroad (India,

China, Egypt, Africa) than at home. In tropical stations, the incidence of chancroid among the British forces is sometimes vastly in excess of that of syphilis. Unofficial reports as to the incidence of chancroid in the American Expeditionary Forces in subtropical and tropical zones reveal that it is twenty times more common than syphilis.

Clinical Signs and Symptoms

The disease begins as a vesicopustule which breaks down rapidly. The pustule soon ruptures leaving a sharply circumscribed, saucer-shaped ulceration. The edges may become ragged and undermined. The base of the ulceration is moist and covered with necrotic grayish exudate. When this is removed, an uneven purulent granulation tissue presents itself. An erythematous halo surrounds the ulcerative lesion. Tenderness is marked, and pain is present. Multiple lesions may develop rapidly by autoinoculation. Systemic reactions are seldom observed.

Clinical Varieties

1. The typical single ulceration may be crateriform or have characteristic undermined ragged edges (fig. 2).
2. Multiple ulcerations (fig. 3) may result from autoinoculation.
3. Transient chancroid (chancre mou volant) consists of a small superficial ulceration which undergoes spontaneous involution without scar formation in 4 to 6 days. Often, 10 or 20 days after the disappearance of the primary lesion there may be an acute regional lymphadenopathy followed by suppuration. This transient or evanescent chancroid is rare and may be confused with lymphogranuloma venereum.
4. The phagedenic type (ulcus molle gangrenosum) is a rapidly destructive form of chancroid disease.
5. The giant chancroid has its origin in a simple chancroid lesion which extends peripherally and is featured by extensive ulceration (fig. 4).
6. The serpiginous type (ulcus molle serpiginosum) spreads by extension and autoinoculation from the original lesions to the groin or thigh. The lesions may spread rapidly. The ulcerations are usually shallow but show no tendency to heal. This form of chancroid may persist for months or years.

Location of Primary Lesion

The lesions occur in the following sites in order of their frequency. In the male: Preputial orifice, internal surface of prepuce, the frenum, the shaft of the penis, and anal orifice. In the female: Labia, clitoris, fourchette, vestibule, anus, and cervix. Spread by autoinoculation may take place anywhere in the perigenital zone, pubis, abdomen, and thighs. Chancroidal urethritis has been observed, and cases of intraurethral chancroid have been recorded.

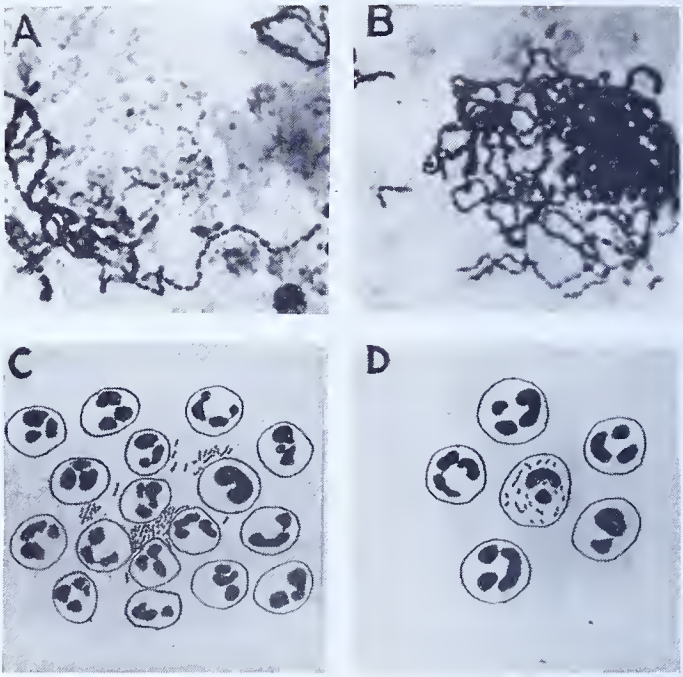

FIGURE 1.—Photomicrograph of spreads from cultures of *H. ducreyi* (*A* & *B*). Note the chain formation of the streptobacilli. Drawing of spreads from chancroidal lesion (*C* & *D*). Note "school of fish" or cluster arrangement of *H. ducreyi* and presence of intracellular bacilli.

FIGURE 2.—Typical chancroidal ulcer.

FIGURE 3.—Multiple autoinoculable chancroidal lesions.

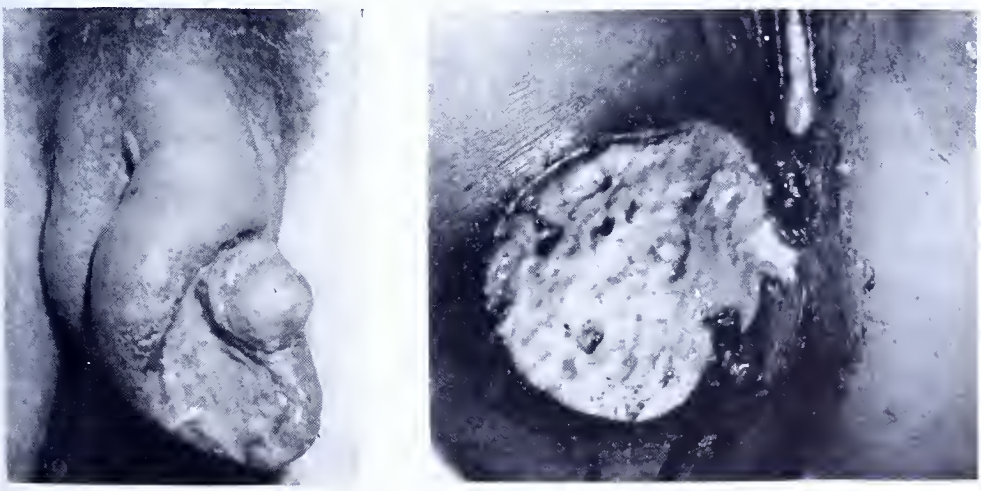

FIGURE 4.—Giant chancroidal lesions in a white male and a Negro female.

Bubo

Chancroid is attended by an inguinal adenitis in over 50 percent of case The typical chancroidal bubo is unilateral, moderately large in size, er thematous, and quite painful. The chancroidal bubo consists of inguina nodes which have become fused and matted together by an acute inflam matory proccss. The mass gradually softens, becomes fluctuant, and unilo ular suppuration results. Spontaneous rupture of the bubo may occu Thc ostium of the ruptured bubo usually becomes a ragged edged, necrot ized, inflammatory ulcerative process.

Inguinal adenitis follows the primary lesion within a few days to weeks. The average interval is 5 to 8 days after the appearance of th primary lesion. Inguinal adenitis tends to subside without suppuratio in more than half of the cases. Bilateral adenopathy is only one-third a common as unilateral bubo formation. Bubo formation is seen almost a frequently in the female as in the male. In the male the site of th primary lesion may have to do with the slightly greater tendency to bub formation, particularly if the lesions are so situated as to produce phimosi and poor external drainage. Occasionally, the primary lesion is a fleetin one that heals spontaneously and 10 to 20 days later is followed by typical bubo.

Extragenital Chancroid

The skin possesses a pcculiar affinity for the bacillus of Ducrey that i not shared by surfaces covered by mucous membranes. This is the reaso for the infrequency of chancroid in the buccopharynx as contrasted wit chancres in that region. A primary extragenital chancroid of the finge with development of an epitrochlear bubo has been reported from ou clinic (*5*). *Hemophilus ducreyi* were grown in pure culture from the pu aspirated from the bubo. Extragenital chancroidal lesions of the umbilicus tongue, lip, breast, chin, and bulbar conjunctiva are on record.

Diagnosis

The diagnosis of chancroidal infection may be aided or determined b one or more of the following methods:

1. Recovery of *Hemophilus ducreyi* from the lesion (*42*).

(*a*) *Spreads.*—Spreads, prepared by rolling the exudate obtained fro the undermined edges of the lesion on a glass slide are stained with eithe Gram, Unna-Pappenheim, Wright or Giemsa stain. It is usually difficul to find the organism in spreads from the opcn lesion because of contamina tion of superimposed infection. It may be necessary to apply moist salin dressings for from 1 to 3 days before satisfactory spreads may be mad Frequently Gram-negative bacilli are found which rescmble the bacillu of Ducrey and suggest the possible but not unequivocal diagnosis. At time

typical streptobacilli distributed in clusters, in leukocytes or in chain formation, paralleling shreds of mucus, may be found which permit a diagnosis of chancroid. The bacilli may be demonstrated more frequently and with a greater degree of accuracy by examining spreads of pus aspirated from buboes. The demonstration of *Hemophilus ducreyi* in spreads from chancroidal lesions is greatly enhanced if Barritt's modification of Pappenheim's Pyronin Methyl Green Stain is used. This modification was intended for the detection of gonococci in spreads and its adaptation for the detection of *H. ducreyi* has proved very satisfactory. The stain may be prepared in the following manner:

Methyl green, aqueous 1 percent (chloroform treated)	100 cc.
Methyl alcohol, absolute	10 cc.
Pyronin G	0. 6 gm.
Phenol	1. 0 gm.
Glycerol	20 cc.

from Barritt, M. M. An improved Pappenheim stain for detection of gonococci in smears of pus. Brit. M. J., 1: 254, 1943.

The methyl green solution is first extracted with one-third volume of chloroform to remove methyl violet which occurs as an impurity. The stain takes immediately. The spreads are fixed with heat. The optimum staining time is one-half to one minute. Pus cells stain bluish green; bacteria, a brilliant red.

(*b*) *Culture.—Hemophilus ducreyi* may be grown in a high percentage of the cases from the bubo pus aspirated under sterile conditions by culturing on agar slants to which 1 cc. of defibrinated human or rabbit blood has been added. Culture of the primary lesion yields a mixed infection, but occasionally *H. ducreyi* may be readily demonstrated.

2. Intradermal reaction.

In this country two tests are in vogue. One in which bubo pus antigen (*11*) is employed and the other in which a bacillary vaccine is used (*17, 27, 28, 65*). The latter is better standardized, gives earlier and more clear-cut reactions (fig. 5).

The skin test is performed on the forearm by injecting 0.1 cc. of the vaccine intradermally. A reaction is positive if an area of 7 mm. of induration appears 48 hours afterward. The reaction usually becomes positive from 8 to 25 days after the appearance of the primary lesion, the average being about 12 to 14 days. The reaction probably remains positive for life. A positive reaction permits a diagnosis of past or present chancroid. A repeatedly negative reaction, particularly if performed after sufficient time has elapsed since the onset of the lesion, is diagnostic in that it rules out past or present chancroid. A false positive reaction may be obtained in patients with stigmas of allergy such as asthma, active moniliasis, or trichophytin infection and occasionally as a coreaction in the acute phase of lymphogranuloma venereum. This coreaction, however, is not as clear cut and on repetition is usually negative

(*6*). A positive reaction in the absence of other positive findings is strongly suggestive, while a repeatedly negative test rules out chancroid.

3. Autoinoculation.

In certain moot cases, autoinoculation is a justifiable procedure (fig. 6). Some of the material obtained from the lesion is rubbed into a previously scarified area on the thigh. In 2 or 3 days tiny vesicopustules usually appear at the site of inoculation, which break down to become the site of a typical chancroidal ulceration. The bacillus of Ducrey can be demonstrated more readily in autoinoculable lesions than in the original ulcers. Recourse to autoinoculation will result often in finding the bacillus in spreads when numerous examinations of exudate from the original ulceration have failed to reveal their presence (*60*).

4. Biopsy.

Histopathologic study of tissue obtained by biopsy may suggest the diagnosis of chancroid although the pathologic changes are not specific. Chancroid is characterized by superficial necrosis infiltrated with polymorphonuclear leukocytes. In the surrounding area, plasma cells, lymphocytes, and endothelial leukocytes are also present. There is acute peri- and endovascultis with pronounced swelling of the endothelium, frequently blocking the lumen of the capillaries and leading to necrosis. The vascular changes are characteristic and are responsible for the superficial necrosis and unhealthy granulation (*54*). Indiscriminate biopsies are not advisable. However, biopsies are of value when bacteriologic methods have failed or when a lesion fails to respond to specific therapy.

5. Exclusion.

A diagnosis of chancroid may be entertained if the signs and symptoms are typical and if repeated search for Treponema pallidum, Donovan bodies, Ducrey bacilli as well as Frei tests and frequent blood serologic tests for syphilis yield negative results, in the presence of a positive Ito (chancroid) skin test.

Complications

1. Mixed chancre: Twelve to fifteen percent of so-called typical lesions are mixed syphilis and chancroid. In its initial stage, the mixed chancre has all the characteristics of a chancroid, but after 15 to 20 days some of the characteristics of a syphilitic chancre may be manifest (*58, 59*). The bacillus of Ducrey may be demonstrated in the early stage when the lesion resembles a chancroid, whereas the Treponema pallidum is found only in the later stage, after 20 days.

2. The possibility of concurrent lymphogranuloma venereum or granuloma inguinale and chancroid must be borne in mind.

3. Balanitis, phimosis, and paraphimosis are frequent and annoying complications.

4. Fusospirochetosis: Superimposed infection with fusospirochetes often leads to marked and rapid destruction of tissue.

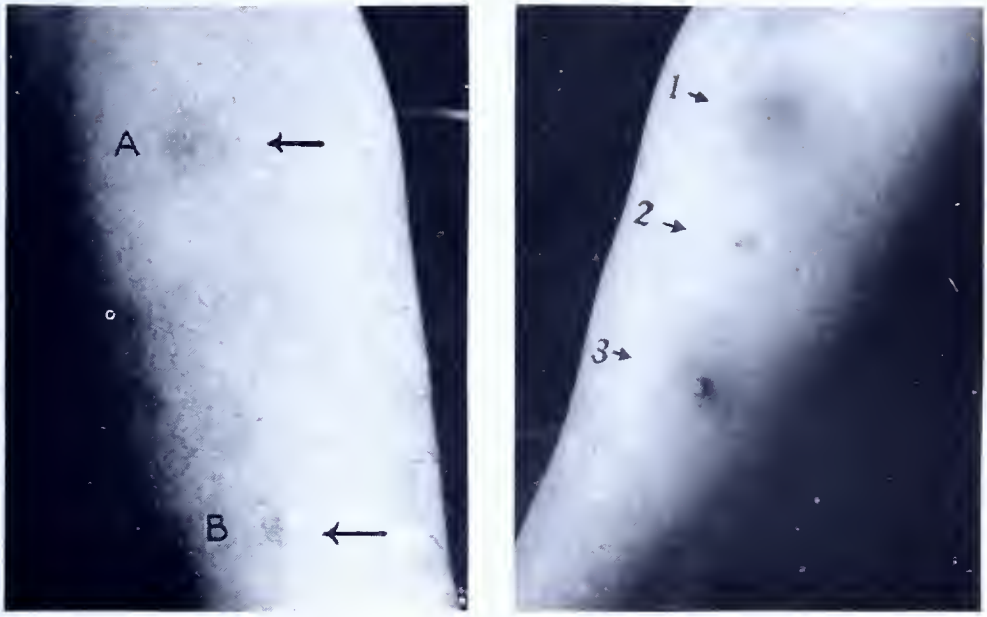

FIGURE 5.—Left: Note the more definite character of the intradermal reaction to chancroidal bacillary antigen (*A*) and the comparatively weaker reaction to bubo pus antigen (*B*). Right: Note the clear-cut intradermal reactions obtained with Dmelcos vaccine (1) and bacillary antigen (3). The control (2) is negative.

FIGURE 6.—Autoinoculation. A drop of pus, aspirated from a chancroidal bubo in right inguinal region (before breakdown of bubo), was injected subcutaneously into left inguinal region, resulting in a typical chancroidal ulcer.

Clinical Course

Usually the disease is a self-limited one and causes only minor discomfort. Systemic reactions are rare or mild. Pain is the most frequent complaint. The primary ulceration may heal gradually or ulcerations may spread by autoinoculation, and there may be much subjective pain and objective inflammation of the affected parts. Phimosis and paraphimosis frequently complicate preputial lesions. Recalcitrant serpiginous ulcerations may result and persist for many months or years without healing. Rapidly destructive phagedenic ulcerations which destroy part or the whole of the glans or a large part of the phallus are not infrequently seen. Giant ulcerations occasionally develop and are very painful; the patient may show toxic symptoms. Inguinal adenitis may be minimal or may progress to suppuration. Complete regression often takes place. On the other hand, the tense, suppurative, and painful bubo may rupture, and either healing will follow within a few weeks or a large, ragged, ulcerative lesion will result at the point of rupture.

Treatment

Until the advent of the sulfonamides, many therapeutic measures were advocated. These varied from topical applications of washes, powders, and ointments to caustics, electric cautery, and surgery. Under such therapy chancroids either healed or progressed in spite of or because of the medication, particularly when surgical means were employed. The dorsal slit to expose a chancroidal lesion was all too common and invariably resulted in chancroidal infection of the cut edges. Circumcision yielded only slightly better results in that circumferential chancroid was more limited in scope.

The sulfonamides (sulfanilamide, sulfathiazole, or sulfadiazine) are specific in the therapy of chancroid (*1, 30, 34, 39, 43*). Sulfathiazole is the drug of choice; the administration of 2 to 4 gm. in divided doses for 7 days is curative in 7 to 12 days in most cases. Occasionally a second course is required. Local applications of sulfathiazole powder or sulfathiazole ointment are not nearly as efficacious if used alone, but may be used as an adjunct to peroral therapy or where there is indication for withdrawal of peroral administration of the drug because of toxicity.

The bubo should never be incised. If fluctuation is present, the bubo should be aspirated with aseptic care, repeatedly if necessary, but never incised. The aspiration point should be dusted with sulfathiazole powder, or a dressing of 5 percent sulfathiazole cream should be applied.

Marked phimosis or paraphimosis may be treated by immersion in hot magnesium sulfate or saline solution, along with a course of the sulfonamides. Circumcision or a dorsal slit is rarely necessary.

Prophylaxis

The routine prophylactic agents generally in use for syphilis and gonorrhea, such as calomel ointment (*48*), silver picrate ointment, argyrol, soap, and water, are probably of little value in the prevention of chancroid. Sulfathiazole ointment in a water miscible base or a 20 percent sulfathiazole—33 percent calomel mixture (*31*) rubbed into the genital zone within 1 to 2 hours after exposure probably afford the best known prophylaxis. Oral sulfonamide therapy administered in doses of 5 to 7 gm. for 1 or 2 days after exposure is an excellent means of preventing the disease (*31, 40*). This method may be used in selected cases, but its widespread employment has many evident drawbacks and is contraindicated in those persons whose loss of precision and skill will not only lessen efficiency but endanger life.

GRANULOMA INGUINALE

Definition

Granuloma inguinale, as the name implies, is a granulomatous process which usually occupies the inguinal region. It is a mildly contagious, chronic, and progressive autoinoculable disease involving skin and corium and occasionally the lymphatics. The well known proclivity of the disease for the external genitalia has earned for it a place in the category of the venereal diseases. Its venereal origin, however, has never been absolutely proved. Granuloma inguinale has been known by a multitude of names such as ulcerating granuloma, granuloma pudendi tropicum, sclerosing granuloma, granuloma inguinale tropicum, granuloma contagiosa, chronic venereal sores, and granuloma venereum. Although granuloma inguinale is possibly not the best name, for it implies that the disease is confined to the inguinal region, nevertheless prolonged and generalized usage has made it the term of choice.

Etiology

The etiologic agent of granuloma inguinale is the Donovan body. Donovan bodies are probably protozoans and are not culturable in vitro by methods used to propagate fastidious bacteria, Rickettsial bodies, and viruses. The disease has been reproduced in humans by inoculation of aspirated pus from pseudobuboes of granuloma inguinale which contained no other organisms than Donovan bodies (*16, 25*). These organisms were recovered in abundance, to the exclusion of other organs, from the experimental lesions that were induced. Attempts to reproduce the disease in experimental animals such as the dog, rabbit, guinea pig, rat, mouse, and hamster have met with failure. The Donovan bodies are strictly tissue parasites of man.

Incubation Period

Little is known about the incubation period of granuloma inguinale The incubation period as recorded in various case reports in the literature varies from 8 days to 12 weeks. In the experimental production of the disease in human volunteers by inoculation of aspirated pus which contained only Donovan bodies, it was difficult to determine the incubation period. Following subcutaneous injection of pus containing the Donovan bodies, a small, localized area of induration developed. This zone gradually increased in size, and in 35 to 45 days localized softening was noted. Subcutaneous abscess with bulging and attenuation of the overlying skin soon occurred, and gradual breakdown and ulceration followed. The classic burgeoning granulation tissue, so typical of the disease was apparent by the fiftieth day.

Epidemiology

Granuloma inguinale is considered generally as a venereal disease, and the consensus is that it is acquired by coitus. The frequency of a history of sexual exposure and the antecedent appearance of a primary penile lesion in the vast majority of males suffering from granuloma inguinale bespeak a venereal origin for the disease. In spite of the fact that the lesions occur chiefly in the genital region, some doubt exists as to its venereal origin. Skepticism may be warranted because the occurrence of conjugal granuloma inguinale is not as frequent as one would suspect, and the difference in racial as well as individual susceptibility stamps the disease as markedly different from the other venereal diseases. Racial immunity and a low degree of contagiousness may account for its rarity in white people and the frequency with which it fails to infect the sexual partner even after repeated exposures. It has been suggested that the presence of the Donovan bodies in the lesions is not primary but is saprophytic upon venereal, traumatic, or other pudendal lesions. Once the Donovan bodies are well established in the tissues, they dominate the local pathologic process, and an exuberant granulation tissue response and progressive destruction result. In considering the fact that most patients with granuloma inguinale have a history of past or coincident venereal disease, the possibility of superimposed infections looms large. On the other hand the type of patient who usually acquires one venereal disease may just as readily acquire another venereal disease. Granuloma inguinale in this country occurs predominantly in Negroes. In many instances its occurrence in white men or women definitely could be traced to sexual exposure to Negroes. This fact, as well as the existence of patients with granuloma inguinale who are free of coincident venereal disease, lend credence to its purely venereal origin.

This disease represents an endemic infection of the poorer Negro classes throughout the southern part of the United States, and the problem

of its endemiologic control are far from being solved. The disease is not necessarily a disease of the Tropics, because it is to be found in American Negroes who have never been exposed to the vicissitudes of tropical life. In short, the disease is indigenous to the United States (*9, 14, 19, 45, 57*).

Racial Incidence

The relative susceptibility of certain races to this disease has been amply demonstrated by reports from reliable investigators both in this country and abroad. In India, for instance, the disease is seen much more frequently in Hindus than in Mohammedans. In two series of cases reported from different sources in India, the incidence of Hindu to Mohammedan was 72 to 1 and 57 to 4, respectively (*50, 47*). In the United States there is an overwhelming preponderance of this disease in the Negro in comparison with the white race. Probably the largest individual series of cases under observation has been reported from New Orleans (*12*). Of 294 patients, 28 were white, a ratio of about 10 to 1. Of some 75 cases studied at the University Hospital Clinic in Augusta, Ga., during the past 8 years, Donovan bodies were found in 3 white patients. The lesion in one instance was on the vulva, was self-limited and healed without therapy.

Age Incidence

The majority of cases observed have ranged from 20 to 40 years of age. This corresponds to the period of greatest sexual activity. The youngest case recorded is that of a 2-year-old white child in whom the disease followed an unhealed circumcision wound (*67*). It appears that the oldest recorded case is that of a 94-year-old man who had recurrent lesions for 15 years. The disease is not inherited, and no instance of congenital granuloma inguinale has been reported so far.

Sex Incidence

An analysis of the sexual incidence of granuloma inguinale reveals that there are nearly twice as many males as females with this disease. Statistical data on this point may vary with different authors, their source of clinical material, and their interests. Several authorities have found the disease more prevalent in the female.

Geographic Distribution

Early reports localized the disease to India and such tropical regions as British Guiana and New Guinea. Isolated reports soon established the fact that the disease was encountered in temperate zones, usually, however, in persons who had traveled in the Tropics. As the entity became more readily recognizable, the endemic nature of the disease throughout various

parts of the world was quickly realized. The disease is found not only in the Tropics and semitropical countries but also in more temperate climates. In truth, the geographic distribution of the disease is from one end of the earth to the other. Cases are being reported from almost every country and zone, from the Equator to Scandinavia. Some idea as to its general distribution may be surmised from the following list of countries from which reports have appeared. *Asia:* India, Ceylon, Siam, Malay States, China; *Australasia:* South Pacific Isles, New Guinea, Australia; *Africa:* Tripoli, Sudan, Morocco, Gold Coast, Cape Peninsula, Madagascar; *Europe:* France, Spain, Germany, Italy, England, Norway; *South America:* Brazil, Argentina, Peru, Venezuela, Uruguay; *Central America:* British and Dutch Guiana, Puerto Rico, Cuba, Costa Rica, Guatemala, West Indies; *North America:* United States, Canada, Mexico.

Clinical Signs and Symptoms

The disease makes its appearance insidiously, without premonitory symptoms or constitutional upset. The disease starts as a vesicle, papule, or nodule. The surface epithelium becomes excoriated or eroded, leaving an ulcer with a beefy red granular base. Early lesions have been observed to be small button-like lesions raised above the surface or a fine granular film covering the glans penis, with occasional nodules gently bulging the surface (fig. 7). An early lesion which is frequently observed is a clean, raised, velvety, smooth tuft of granulation tissue situated at the mucocutaneous border of the vaginal orifice, at the preputial orifice, or on the glans or inner surface of the prepuce. The margin of the lesion is sharply defined. The primary lesion in the female is usually found on the vulva or vagina. Occasionally, it is found on the cervix or in the perigenital zone. The granulation tissue, if traumatized, bleeds easily. The lesions are not painful, which accounts for the fact that patients rarely seek medical care early in the course of the disease. The inguinal manifestations are secondary to the genital lesions. Occasionally, inguinal lesions appear without trace of a genital lesion, although a history of a previous genital lesion which healed spontaneously is frequently obtained.

Clinical Course

The lesions show very little tendency to heal; they spread by continuity or contiguity. Extension is often slow, showing only insidious progress. Occasionally, the spread is more rapid, and there is a predilection for moist contact surfaces particularly in the cruroscrotal folds. Daughter lesions frequently develop near the larger lesions. These coalesce after a time to form extensive ulcerative processes. The advancing border of the lesion has characteristic rolled edges, the granulation tissue piling over onto the bordering epithelial surface (fig. 8).

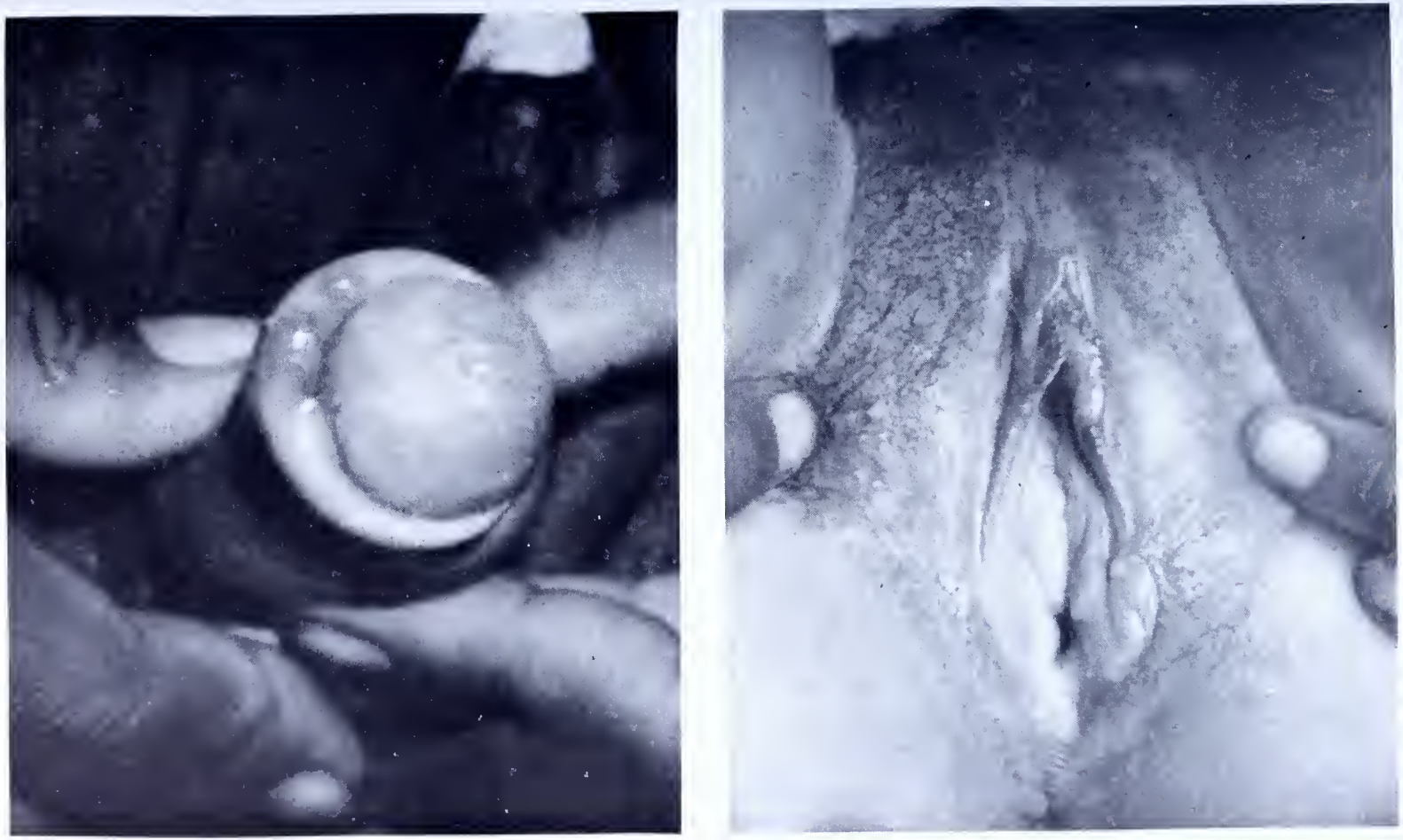

FIGURE 7.—Examples of early granuloma inguinale in the male and female.

FIGURE 8.—Extensive lesion and daughter lesions of granuloma inguinale.

The ulcerative process may reach a stage where it remains more or less stationary for many years. Secondary pseudoelephantoid enlargement of penis, scrotum, or labia may occur. The lesions may show a tendency to scar formation at one margin and chronic progression at another. Exacerbations of progression are common and sometime so extensive as to occupy great surfaces. The lesions, when present for several months to years, have a sour-smelling, peculiarly pungent, characteristic odor. Ultimately, in many instances, marked impairment of general health occurs and anorexia, anemia, and debility develop, ending in extreme cachexia and death.

Clinical Types

Exuberant.—The ulcerative process is covered by a hypertrophic, vegetative granulation tissue, which is soft and velvety to the touch and beefy red in appearance. The edges are rolled, raised above the surface, and the margins are never undermined. The granulation tissue bleeds easily on traumatization and can be curetted or scraped off, leaving a shallow, granular base.

Ulcerative.—The lesion may appear as an ulcerative process, covered by a foul smelling, membranous exudate. These lesions are apt to be somewhat painful. The lesions may be ulcerative in type from the start but usually result when the exuberant type of lesion becomes secondarily infected and markedly contaminated with other organisms, particularly fusospirochetes.

Cicatricial.—A chronic cicatricial type of granuloma inguinale is occasionally encountered in which the granulomatous process attempts to heal itself. Where healing seems to have taken place, the area is slightly elevated or bulging and is covered by depigmented epithelium or scar tissue. Small scarred granulomatous lesions are scattered irregularly at the periphery of the progressive scar. The attempted healing is a keloid type of change. Donovan bodies may be found in tissue sections taken through the scarred zone.

Pseudobubo of Granuloma Inguinale

Buboes are seen with frequency in chancroid and lymphogranuloma venereum, less frequently in the other venereal diseases. The bubo has been defined as a suppurative adenitis and is always secondary to a primary focus in the genital zone. In granuloma inguinale, the inguinal lesion in most instances follows one on the external genitalia. The classic burgeoning inguinal granulomatous ulceration that is so frequently observed is preceded by a localized indurated swelling or fluctuating abscess which simulates a bubo prior to rupture or incision (fig. 9). Traditional teaching has repeatedly emphasized that granuloma inguinale is a disease of the skin and corium and not of the lymphatics. The demonstration of

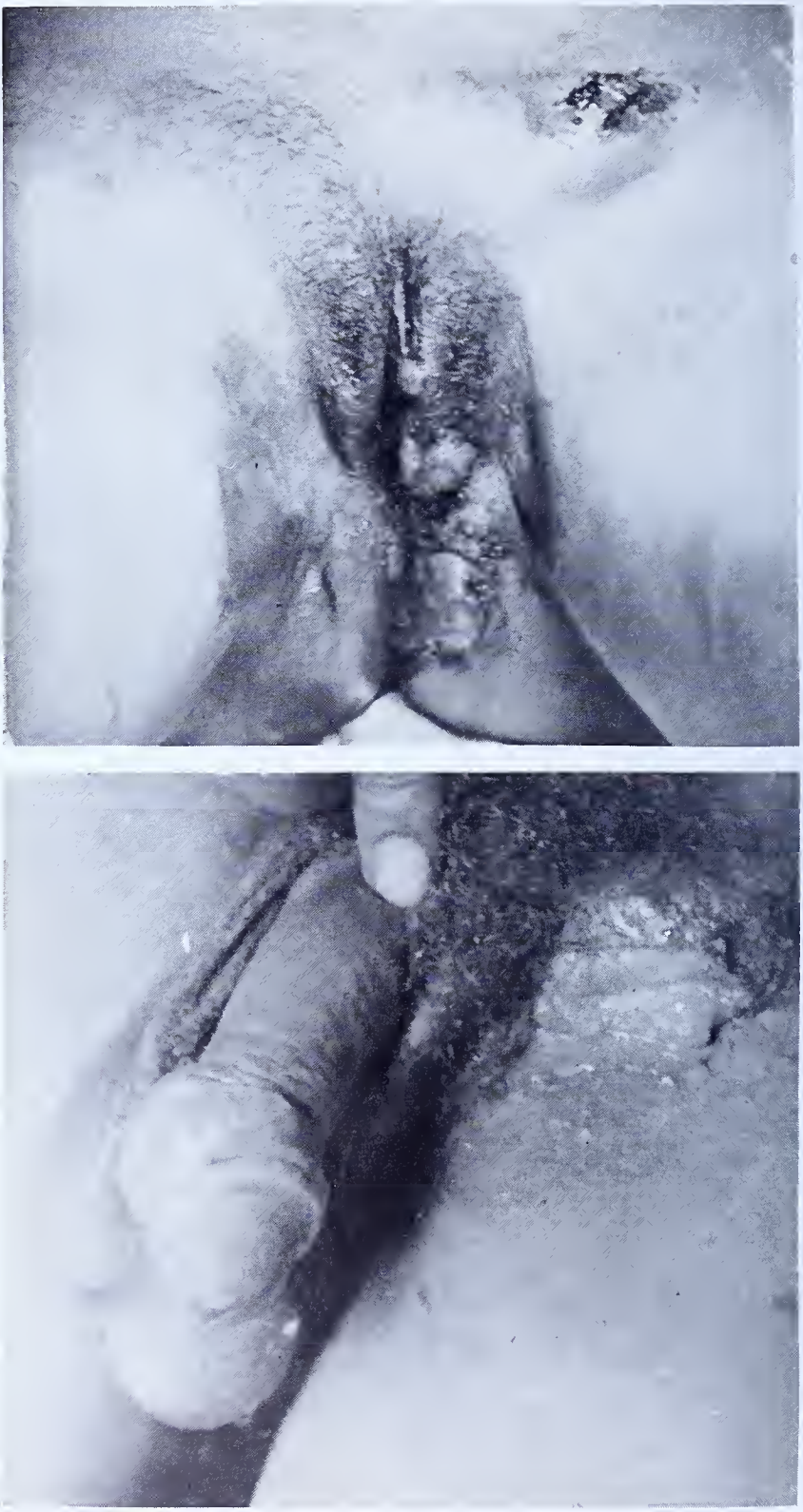

FIGURE 9.—Pseudobubo of granuloma inguinale. *A*. Granuloma inguinale o pudendum of 2 years' duration followed by inguinal pseudobubo. Photograph day following aspiration of inguinal abscess with recovery of Donovan body i pure culture. *B*. Note primary lesion on penis and recently ruptured inguina pseudobubo.

the pathognomonic cells of granuloma inguinale in regional lymph nodes showing mild focal reactions and perilymphadenitis reveals the fallacy that has been preserved in the literature as to lymphatic involvement. The frequency with which the disease gains a foothold in the inguinal region following primary infection is understandable. Autoinoculation may account for many such occurrences. However, when an inguinal swelling precedes the typical inguinal lesion, it is probable that the lymphatics played a role in the dissemination of the disease. Excised tissue from such inguinal lesions studied microscopically reveals a diffuse granulomatous reaction in the papillae, corium, and subcutaneous tissues and is not comparable to the adenitis found in venereal lymphogranuloma, chancroid, or syphilis. Hence the term "pseudobubo" to describe the indurated inguinal swelling or suppurative abscess that so frequently follows a primary focus on the external genitalia in granuloma inguinale. It is not an adenitis per se but a subcutaneous granuloma, although the underlying lymph nodes reveal a moderate endothelial hyperplasia and at times focal reactions with pathognomonic cells.

Location

The lesions of granuloma inguinale occur in the following anatomic sites in order of their frequency:

(1) External genitalia.

a. In the male—glans, prepuce, shaft of penis (without inguinal involvement).
b. In the female—labia minora, labia majora, clitoris, vaginal orifice.

(2) Inguinal region alone or along with primary genital lesion.
(3) Perineum, anal region, buttocks.
(4) Cervix uteri (*52*).

Extragenital Lesions

Most of the extragenital lesions are secondary to pudendal lesions although in a few instances purely extragenital lesions have been described. Extragenital lesions occur in about 6 percent of all cases of granuloma inguinale (*32*). The parts affected that have been recorded in the literature include the oral cavity, lips, throat, neck, nose, chest, cheek, thorax, and liver. Patients with extragenital lesions usually give a history of granuloma inguinale of long duration (fig. 10). In our series of some 75 cases there were 4 instances of extragenital lesions. In 1 patient the multiplicity of lesions scattered over the neck and chest suggested metastatic foci rather than autoinoculable lesions. This occurrence of purely extragenital lesions such as chronic leg ulcers, or following traumatic lesions, lends support to the contention that granuloma inguinale may be due to a secondary contaminant (*66*).

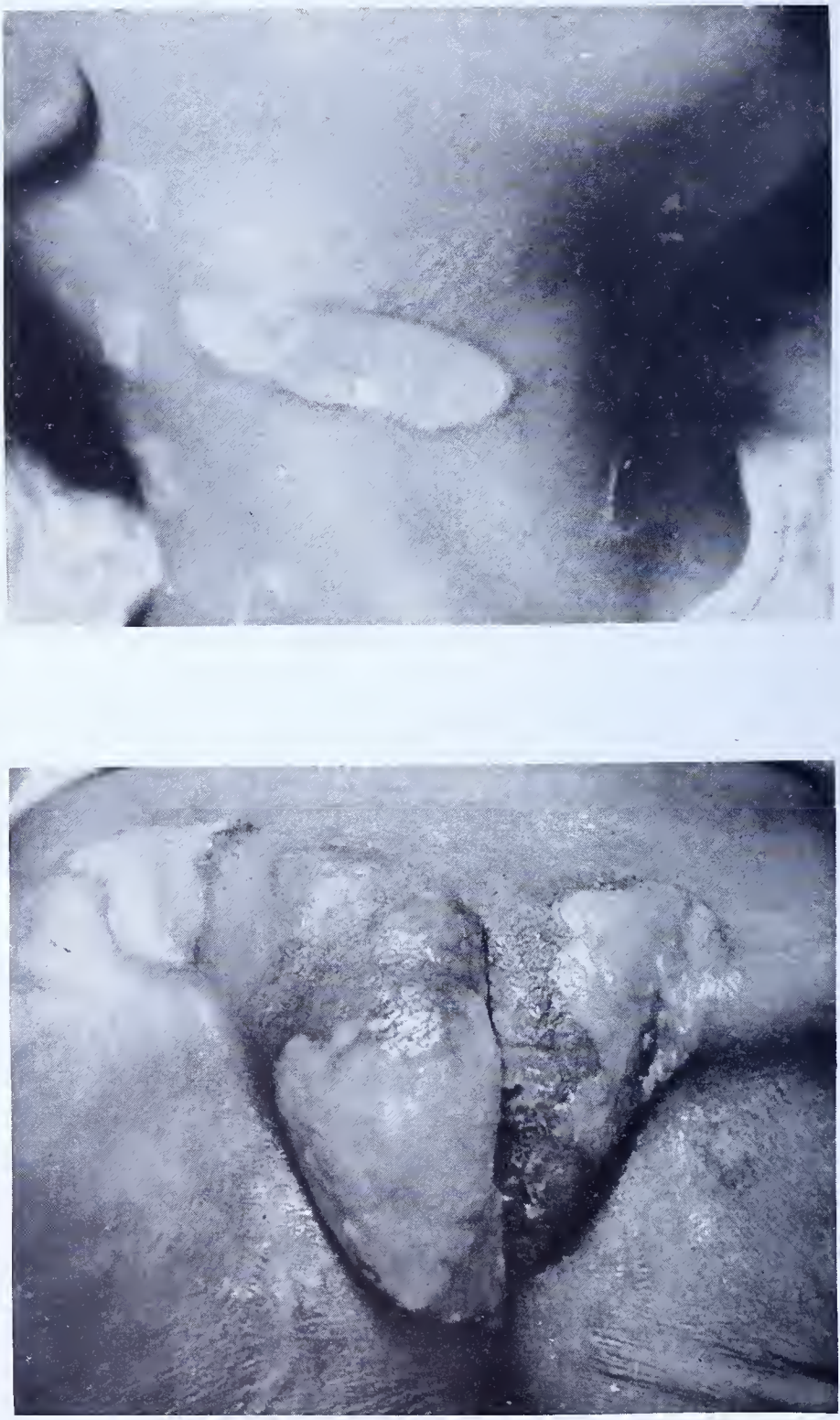

FIGURE 10.—Extragenital and genital granuloma inguinale.

Granuloma inguinale reveals in the pure or unmixed cases a uniform histologic picture. The essential features are (a) the massiveness of the cellular reaction in which the luxuriant granulation tissue is surcharged with plasma cells, (b) the relative and conspicuous paucity of lymphocytes, (c) the diffuse sprinkling of polymorphonuclear leukocytes, with focal collections in the superficies and papillae, (d) the pronounced marginal epithelial proliferation simulating early epitheliomatous changes, (e) the pathognomonic large mononuclear cells scattered in various numbers throughout the granulation tissue (fig. 11–*A*).

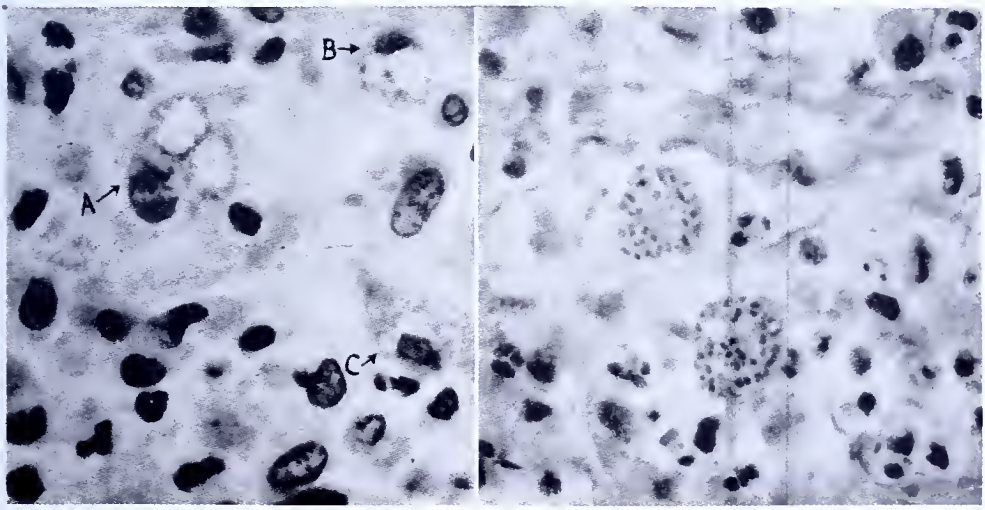

FIGURE 11.—*A*. The characteristic cellular response as observed in tissue section stained with hematoxylin and eosin. A, the pathognomonic cell is diagnostic of granuloma inguinale. Note the small rounded bodies lining the periphery of the intracytoplasmic cysts. B and C, pathognomonic cells slightly out of focus. ×2250.

B. A biopsy section stained by Dieterle's silver technic. Note the characteristic closed safety pin appearance of some of the so-called Donovan bodies filling the intracystic spaces of the pathognomonic cells. ×2250 (Pund's method).

The pathognomonic cell is specific for granuloma inguinale. The relatively large size of the cell, the diameter of which varies from 25 to 90 microns, and the many intracytoplasmic cysts filled with deeply stained bodies are its cardinal features. Donovan bodies are round or rod-like, are grouped within the cysts and have an affinity for hematoxylin. Their recognition is of paramount importance because it permits the diagnosis of granuloma inguinale to be made by histologic study of the tissue (*53*).

The affinity of the intracystic bodies for silver salts facilitates the recognition of the characteristic cell (*52*). With silver these bodies are stained black to brown and have a closed safety pin appearance due to their elongated ovoid and intense bipolar staining reaction (fig. 11–*B*).

The life cycle of the Donovan body of granuloma inguinale in th host's tissue is apparently a simple one. The organism invades the larg mononuclear endothelial cells of the infected tissue until the cell is eventu ally destroyed and new cells are invaded. Occasionally, neutrophili leukocytes and perhaps the mononuculear leukocytes phagocytize and de stroy the extracellular encapsulated parasites, but the invasion of the larg mononuclear endothelial cells occurs more rapidly than does phagocytosis so that eventually more tissue is infected. The parasites reproduce b multiple segmentation or schizogony in the large mononuclear endothelia cells. Sometimes there may be as many as six foci of reproduction within one large mononuclear cell. The immature bodies resulting from multipl segmentation mature within cystic spaces created in the parasitized cell until each organism is fully developed and apparently encapsulated. The infected cell finally ruptures and the mature Donovan bodies are liberated (fig. 12). The tinctorial features of the mature encapsulated body are

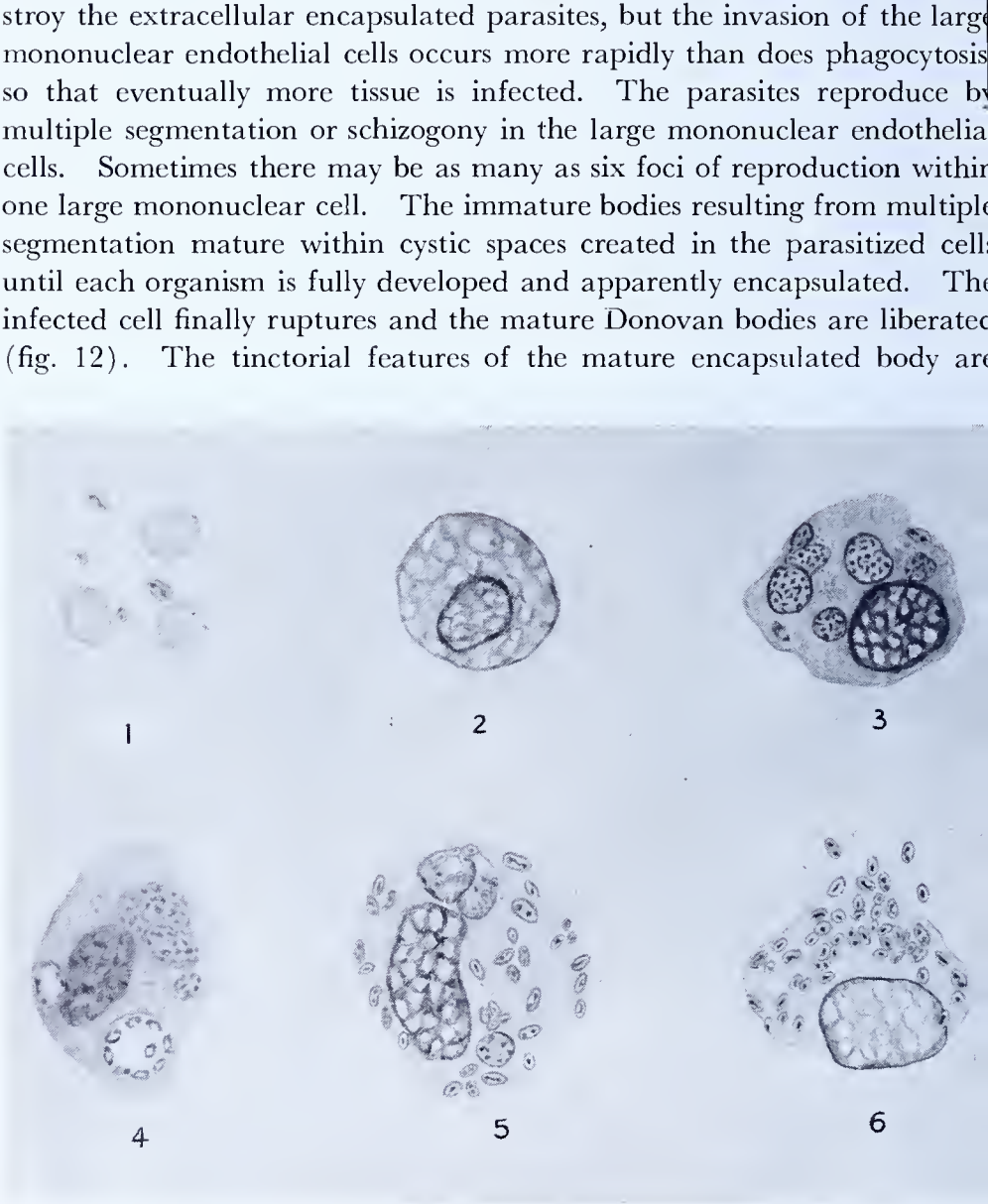

FIGURE 12.—Camera lucida drawings to illustrate possible life cycle of Donovan bodies (Dienst), reduced from a magnification of 1,500 diameters: 1. Mature extracellular organisms with red blood cells. 2. Large mononuclear endothelial cell showing early invasion with Donovan bodies. 3. Infected cell showing multiplication of immature parasites in cystic spaces. 4. Further multiplication and maturation of parasites in monocyte. 5. Individual organisms becoming mature. 6. Mature encapsulated Donovan bodies escaping from ruptured and disintegrating monocyte.

easily demonstrated with Wright's stain. The capsule stains pink, the metachromatic bars or nuclei stain blue and black. The size of the mature ovoid encapsulated body measures about 1 to 1.5 microns in length and 0.5 to 0.7 microns in thickness.

The encapsulated form is the most resistant stage of the parasite; it can be demonstrated by Wright's stain in the specific exudate stored 4 weeks in the ice box. The encapsulated form is also the last to disappear after attempted cultivation in vitro.

Complications

Fusospirochetosis is the most common complication of granuloma inguinale. The lesions become ulcerative, progressive, foul smelling, and painful and are often refractive to specific therapy. Syphilis, chancroid, and lymphogranuloma venereum may be coexistent. Occasionally, superimposed malignancy has been found to complicate the picture. Secondary elephantoid enlargement of the penis, scrotum or vulva, and clitoris may occur.

Diagnosis

The clinical picture may be so classical, the exuberant beefy red velvety tufts of granulation tissue so striking that the diagnosis is unmistakable. Nevertheless, granuloma inguinale should be diagnosed only when Donovan bodies are demonstrated in spreads or when histologic study of biopsy reveals the pathognomonic cell.

Spreads.—Spreads are made by obtaining a minute piece of granulation tissue from the surface of the wound, if it appears to be clean, or from the deeper part of the lesion, if it appears to be markedly infected. The exudate covering the infected lesions should first be removed. The small piece of granulation tissue is best obtained with a sharp instrument such as a small bone curette. The tissue obtained is smeared along several glass slides or crushed between two slides and then spread along the slide. The slides are then dried and stained. Wright's stain has proved most satisfactory but Giemsa stain may be used to equal advantage. The demonstration of Donovan bodies is possible in every case of granuloma inguinale but may occasionally prove difficult for the following reasons:

1. They may be scanty on the surface and demonstrable only when spreads are taken from a deep part of the lesion.

2. Because of their pleomorphism they may not be readily recognized. In their atypical immature nonencapsulated forms they may resemble other organisms. The presence of coccoid, diplococcoid, or bacilli-like organisms surrounded by a distinct halo and lying within cystic spaces of monocytes is suggestive of the immature forms. When such organisms are present, diligent search will reveal some mature encapsulated forms (fig. 13).

3. The superimposed infection may be so overwhelming as to veil their presence.

Biopsy.—The above handicaps may be overcome by resorting to histologic methods when spreads fail to corroborate the clinical diagnosis. Paraffin sections of biopsy material stained with hematoxylin (Delafield's) and eosin or by Dieterle's silver technic will demonstrate the pathognomonic cell and the characteristic inclusion bodies with moderate ease in all cases of granuloma inguinale. Histologic study is most revealing when the material is obtained at the margin of the lesions or where granulation tissue appears healthiest or cleanest.

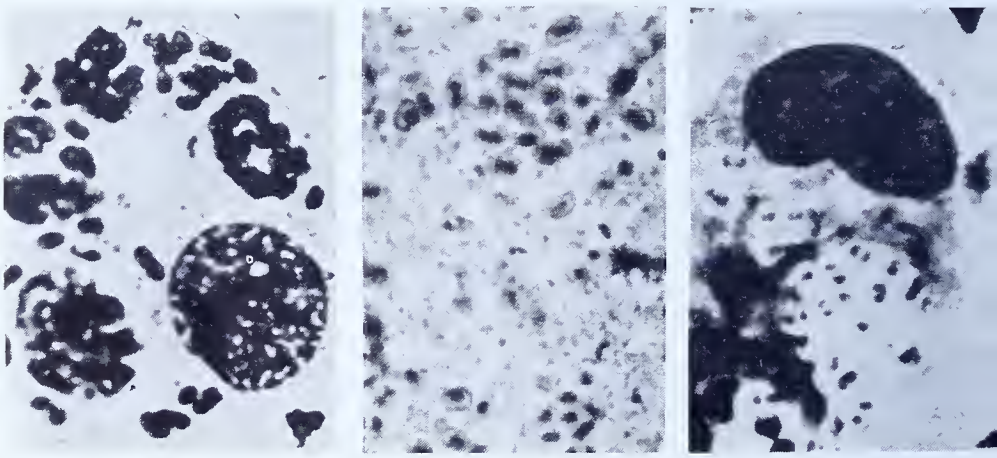

FIGURE 13.—*A.* Degenerative deeply stained encapsulated Donovan body within cytoplasm of mononuclear cell. *B.* Mature encapsulated Donovan bodies lying free in tissue spaces. *C.* Immature nonencapsulated Donovan bodies lying within cytoplasmic cysts of mononuclear cell (DeMonbreun and Goodpasture).

TREATMENT

Chemotherapy.—The effectiveness of chemotherapy decreases in direct proportion to the chronicity of the lesions. Early granuloma inguinale responds rapidly to therapy with various antimony preparations. Tartar emetic (1 percent) may be given intravenously in ascending doses beginning with 1 cc. and increasing the dose by 1 cc. until a dose of 10 cc is reached. It is administered every 2 or 3 days. When the maximum is reached the dosage is decreased by 1 cc. in descending strength until it is reduced to the initial dosage. After a 2-week rest period medication is again started. Toxic manifestations such as joint pains, sore gums, anorexia, nausea, and vomiting, are often encountered with tartar emetic. Freshly prepared 1 percent solutions are said to be more effective than stock ampules (*61*).

Fuadin (Winthrop) has proved to be superior to tartar emetic. It is more convenient to administer, and toxic reactions are seldom encountered. The solutions are stable and are available in 1.5, 3, and 5 cc. ampules

The initial dosage of Fuadin is 1.5 or 3 cc. intramuscularly. The dosage is then raised to 5 cc. and given three times per week. Anthiomaline (Merck) is another stable and useful preparation that yields good results in a high percentage of cases. It is available in 3 cc. ampules and is administered intramuscularly three times per week. When lesions remain refractory to treatment with one preparation, a change to another antimony compound is recommended. Usually definite improvement in the lesions may be noted within 4 to 6 weeks. Either Fuadin or Anthiomaline should be continued until healing is complete. Medication should then be administered at weekly intervals for a period of 6 months if recurrences are to be avoided.

Some of the early cases and particularly the chronic cases of 2 to 3 years' duration or longer may prove chemoresistant. If the lesions are localized they may be excised surgically. If the lesions are extensive, several courses of radiation therapy should be administered. The dosage should be similar to that employed in the treatment of skin cancer. Chemotherapy should be administered along with radiation therapy. Complete scarring and healing may be expected. The patient should be exhorted to continue with chemotherapy for 6 months after cessation of X-ray therapy to lessen the chance of recrudescence.

Chemoresistant and recalcitrant cases may harbor a superimposed fusospirochetal infection. It has been noted that treatment directed against these saprophytic organisms renders the lesions susceptible to further antimony therapy. Fusospirochetosis may be treated by sodium perborate dressings or by applications of a mixture containing equal parts of zinc peroxide and cod-liver oil. Intravenous arsphenamine therapy is of no value, although topical application of the arsphenamines is useful in eliminating the fusospirochetal infection. Recently, the application of a suspension of 20 percent podophyllin in olive oil to recalcitrant lesions for 5 to 7 days has been recommended along with chemotherapy by antimony compounds. Preliminary therapy designed to rid the ulcers of secondary infection consists of hot sitz baths and daily cleansing with hydrogen peroxide. After the course of podophyllin therapy is concluded, scarlet red ointment is substituted (*75*).

Prognosis

Cure may be obtained in practically every case of granuloma inguinale when the diagnosis is made within the first 6 months of the infection. Over 50 percent of patients with lesions of several years' duration will respond, although more slowly, to treatment. Recurrences in this group are very frequent. Neglected or therapy-resistant patients may harbor the disease for 10 to 15 years. With increasing age, declining health and resistance, there is a gradual activation of the lesions. The ulcerations become so extensive as to occupy the whole pudendal region, lower part

of the abdomen, buttocks, and thighs. The patient becomes anemic bedridden, cachectic, and finally dies.

LYMPHOGRANULOMA VENEREUM

Definition

Lymphogranuloma venereum is a virus disease acquired venereally and i characterized by a small evanescent initial lesion somewhere on the geni talia which is frequently followed by a subacute regional lymphadeniti and/or a chronic inflammatory neoformative reaction in the subjacen connective tissues of the infected parts. The disease is also known by such names as lymphogranuloma inguinale, Nicolas-Favre disease, porade nitis, and lymphopathia venereum. It is a disease of the lymph channels and lymph nodes and may be manifest in a variety of ways, mainly by bubo formation, rectal stricture, genital elephantiasis, and ulceration (*15, 18, 21, 69, 71, 78*).

Etiology

The causative agent of lymphogranuloma venereum is a filterable virus (*37, 44*). Until recently it was assumed that the virus was ultramicroscopic. It has been shown, however, that the agent is not ultramicroscopic; several developmental phases may be seen under the microscope (*55*). The cells of the yolk sac of the developing embryo are readily infected with the agent of lymphogranuloma venereum, and the virus bodies can be observed in these cells when subjected to special stains. Cytoplasmic inclusion or Gamna bodies have been noted in mononuclear cells from infected lymph nodes varying in size from those which are barely visible to others 4.5 microns in diameter. The virus of lymphogranuloma venereum more closely resembles the pathogenic agent of psittacosis than the characteristic viruses such as poliomyelitis, choriomeningitis, or vaccinia. Unlike the characteristic viruses, the agent of lymphogranuloma venereum in some measure is susceptible to chemotherapy with the sulfonamide drugs and in this respect is allied to the so-called virus diseases of trachoma and inclusion blenorrhea (*56*).

Incubation Period

The primary lesion usually appears from 5 to 21 days after the infective coitus. Probably an incubation period of 7 to 12 days is most usual. Frequently the first manifestation of the disease is the inguinal bubo. The primary lesion is often so transitory or hidden as to escape notice. The inguinal bubo usually appears from 10 to 30 days after exposure, although at times several months may elapse.

Epidemiology

The disease is contracted by sexual intercourse and occasionally through homosexual practices. It is widespread throughout the world but is met

with greater frequency in tropical and semitropical climates. In the United States it is endemic in the Southern States, particularly among Negroes. The age incidence corresponds to the period of greatest sexual activity, but children may contract the infection by simple contact from bedfellows, douche nozzles, or infected clothing. It is not believed to be acquired congenitally.[1] The disease occurs among all races exposed to the infection and is commoner among people with promiscuous habits and those who have had one or another of the venereal diseases. Occupation per se must be considered in its epidemiology, for in men the disease is seen with comparative frequency among sailors, and in women, among prostitutes. As long as a contaminating exudate is present, whether it be in the form of a proctitis, urethritis, discharging sinus, or an open ulcerative lesion, the disease must be considered as contagious.

Incidence

Exact data are not available on the incidence of lymphogranuloma venereum in this country since in some States it has become a reportable disease only recently. A high proportion of positive reactions to the Frei or complement fixation tests are observed in patients who have had one or another venereal disease although they showed no clinical evidence of lymphogranuloma venereum. In one of the clinics at the University Hospital 197 patients with manifestations of lymphogranuloma venereum were observed over a 5-year period.[2] This did not include cases with coincidental positive Frei reactions but only those patients who had either buboes, rectal strictures, genital elephantiasis or some definite stigma of the disease at the time of observation. Of this number 13 were white patients, giving a racial incidence of about 16:1. The incidence of lymphogranuloma venereum in the armed forces for the period 1936 to 1940 reveals that lymphogranuloma venereum on the average is one-fifth to one-tenth times as common as chancroid, and that both diseases are far more prevalent in the Navy than in the Army (chart 1).

Sex Incidence

The nature of the epidemiology of the disease should argue against a differential sex ratio. The reported sex incidence has favored the male. However, in our clinics, because of the chronicity and anatomic vagaries of the disease that are peculiar to the female, greater incidence in the female has been observed (chart 2).

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[1] This point is open to question. Lymphogranuloma virus is transmitted in pregnant mice via placenta into the fetus. There are some cases on record where the child born of a mother with lymphogranuloma venereum reacted positively to the Frei test. Although we have not been able to confirm this, it is conceivable that pregnancy during the active phase of this disease could prove infectious for the fetus in utero.

[2] Statistics do not include patients seen in other clinics, only those observed in the Granuloma Clinic.

CHART 1.—*Rate of admissions for chancroid and lymphogranuloma venereum per 1,000 mean strength—U. S. Army and U. S. Navy*

Year	Army		Navy	
	Chancroid	Lymphogranuloma venereum	Chancroid	Lymphogranuloma venereum
1936	5.3	0.1	9.75	0.8
1937	4.3	.4	7.82	1.1
1938	2.5	.5	10.49	1.8
1939	2.4	.4	13.08	2.1
1940	4.1	.5	11.72	1.5

Data from: Annual Reports of the Surgeon General, U. S. Army, 1937–41; Statistics of Diseases and Injuries in the U. S. Navy, 1936–40.

CHART 2.—*Age and sex incidence of lymphogranuloma venereum in 197 consecutive cases*

Age	Male	Female	Age	Male	Female
0–10	0	2	41–50	5	
11–20	19	16	51–60	1	
21–30	44	59			
31–40	10	28	Total	79	11

Location and Character of Primary Lesion

In the male, the commonest sites are the coronal sulcus, prepuce, glans and urethra. In the female, the primary lesion may appear on any part of the external genitalia, but the most usual site is the posterior vaginal wall or the neighborhood of the fourchette. The inoculatory lesion usually consists of either a small erosion, an infiltrated papule, or a herpetiform vesicle or ulcer. The lesion is usually single, rarely multiple, with clean-cut edges surrounded by a reddened zone without induration or infiltration. In both male and female the primary lesion usually remains unnoticed, particularly in the former when it occurs beneath the prepuce. It is painless and so transient that few patients with lymphogranuloma venereum are ever aware of a primary focus. When patients have noticed the inoculatory lesion they describe it simply as a hair-cut, a tiny blister, or a pimple. Soon after the disappearance of the primary lesion and coincident with the appearance of the inguinal bubo, an ulceration may be present on the genitalia which frequently is mistaken for the inoculatory lesion but which in reality is a secondary manifestation (fig. 14).

Clinical Symptomatology

The lymphotropism of the virus leads to the development of an adenitis in the drainage area of the primary lesion. When the primary lesion occurs in the inguinal lymphatic drainage area, whether in male or female, the characteristic inguinal bubo usually follows. The anorectal component is an inevitable sequel in both sexes when the perirectal glands are involved

FIGURE 14.—Evanescent primary lesion (*A*) of lymphogranuloma venereum which was followed in 3 weeks by an ulceration on the shaft of the penis simultaneous with bilateral buboes (*B*).

either by direct or retrograde extension of the infection. Its occurrence in the female is far more common because of the lymphatic drainage from the vagina, resulting in lymphatic spread of the virus towards the perirectal glands.

Constitutional symptoms are often present during the stage of lymphatic progression of the infection, particularly during lymph node involvement. Fever, chills, headache, vague abdominal aches, joint pains, and anorexia are commonly encountered. Occasionally, such severe manifestations as meningism or a typhoidal state supervene. Splenomegaly is met with sometimes (*33*).

CLINICAL VARIETIES

Inguinal syndrome.—At an early stage a simple, discrete, movable, tender gland is present in the inguinal region. After advancing for some days the inflammatory process may come to an end or may progress to involve all the nodes of the group with considerable periadenitis. A firm, bulging swelling makes its appearance and is either lobulated, oval, or markedly elongated. The skin is adherent and has a purplish hue. Irregular areas of softening usually develop, and suppuration through multiple fistulous tracts may occur. Occasionally, the suppurative process forms a more or less indurated but unilocular abscess. Sometimes the bubo remains firm, nodular, and indurated, for many months. The inguinal adenopathy is usually unilateral but occurs bilaterally in one-third of the cases. In about 20 to 25 percent of patients with inguinal buboes, complete regression of the swelling occurs. Femoral buboes are encountered occasionally.

Genital syndrome.—In the male, secondary ulceration of the penis and occasionally massive elephantiasis of the penis may occur (fig. 15). Bubonuli, i. e. small abscesses along the course of the lymphatics of the penis

FIGURE 15.—Massive elephantiasis of penis due to virus of lymphogranuloma venereum.

FIGURE 16.—Esthiomene—elephantiasis and ulceration of vulva and lobulated anal growths.

are occasionally observed. In the female, elephantiasis vulvae or clitoridis is very common, particularly in Negroes. Hyperplasia and hypertrophy of the vulvar tegumentary and subjacent connective tissue layers, concomitant with local lymph stasis and dilatation of the lymph channels are responsible for the syndrome of elephantoid growths and ulcerations of the vulva and perianal region. This syndrome is frequently referred to as esthiomene (fig. 16). One labium or the preputium clitoridis may be enlarged or both labia minora and majora may be involved. The surface of the enlarged and swollen parts may be smooth or verrucose, polypoid, or ulcerated. The chronic inflammatory neoformative reaction leads to swellings that are turgid and rubberlike in consistency. Pedunculated tumors of the labium or clitoris are seen quite frequently. Vaginal stricture or rectovaginal fistulae are sometimes encountered.

Anal syndrome.—Polypoidal and lobulated growths about the anal orifice occur either alone or along with a genital or rectal syndrome. In the early stages of this syndrome, indurated rubbery anal tabs are present and may be mistaken for hemorrhoidal tags.

Rectal syndrome.—Rectal stricture is frequently found without other manifestations of lymphogranuloma venereum and often in the absence of a history of a primary lesion or bubo. On the other hand, a history of a bubo may be obtained some time before the development of rectal symptoms. The stricture is usually of the cylindric "rubber hose" variety. It is usually situated several centimeters above the anal orifice. The length of the average stricture is about 4 cm. although annular constrictions as well as strictures that are about 10 cm. in length are encountered. The lumen may be so narrowed as to admit the examining finger with difficulty. On palpation the walls of the lumen present an indurated and at times semirigid surface. Strictures are progressive, and with further constriction of the lumen there is increasing constipation and difficult passage of stools. Many patients with rectal stricture are troubled with pain and a purulent discharge. Occasionally, bloody stools and rectal hemorrhages occur which lead one to suspect malignancy. Rectal strictures are not the only sequelae to perirectal lymphatic involvement or direct implantation of the infective agent on the rectal or anal mucosa. Such conditions as a swollen, redundant indurated rectal mucosa, proctitis, rectal granuloma, polypoid and verrucous hypertrophy of the mucosa are occasionally encountered. Involvement of the perirectal tissue causes perirectal abscesses resulting in ischiorectal abscesses or chronic anal fistulae. Strictures and ulcers of the rectum may extend upward to involve the sigmoid and isolated parts of the large intestine to simulate ulcerative colitis.

Urethral syndrome.—Nonspecific urethritis has been a diagnosis made with a great deal of reluctance. Stained spreads of urethral discharge which fail to reveal incriminating organisms but show an abundance of leukocytes-suggest a diagnosis of lymphogranuloma venereum. Urethral

strictures and fistulae may occur.[3] In the female, swelling and ulcer tions of the urethra or papillary elevations of mucosa about the urethr meatus have been observed.

Bubo

The bubo of lymphogranuloma venereum may resemble the unilocul abscess of chancroid. At other times it may resemble the firm, rock-li induration of syphilitic bubo. Most often, however, the bubo of lymph granuloma venereum has certain characteristics which distingush it fr buboes of the other venereal diseases. The inguinal mass consists of ma discretely enlarged lymph nodes held together by a plastic periadenit In each of these nodes that comprise the bubo the inflammatory rea tion is far from uniform. In one node there may be active suppurati with softening and abscess formation while in the neighboring node su a process may be only in its early stages. This accounts for the alternati areas of softening and induration. When breakdown occurs, draina takes place from individual zones, and this accounts for the multiple f tulous tracts in lymphogranuloma venereum. The ostia of such fistul show no inflammatory reaction or tendency to ulcerate as in chancroi The characteristic bubo of lymphogranuloma venereum is lobulated ar elongated, with the long axis parallel to the groin fold. The enlargeme of the nodes above and below this fold gives the bubo a grooved a pearance. This sign of the groove is practically pathognomonic of lymph granuloma venereum (fig. 17). The interval between the infecting coit and the development of adenitis varies from 10 to 30 days although some instances the bubo does not appear until 2 or 3 months afterwar In an 11-year-old girl with a history of forced coitus (rape) the bu appeared 1 month later.

Extragenital Lymphogranuloma Venereum

Axillary buboes have occurred in physicians through accidental infecti of the finger or hand. Laboratory workers who are constantly exposed high concentrations of the virus have developed generalized systemic infe tions with symptoms which are rather characteristic, i. e., fever, chil sweats, articular rheumatism, and headache. Cases of conjunctivitis d to the virus of lymphogranuloma venereum have also been reported laboratory workers. Submaxillary and related lymph node involvem can occur by infection through perverted sexual practices.

Clinical Course

The clinical course of the disease varies from one person to anothe In one the disease may be so minimal that the patient is never aware

[3] Recently a case of urethral stricture with fistulae was observed in a white male. He ga a strongly positive Frei reaction and a history of a bubo several years previously, while h wife had a characteristic rectal stricture.

FIGURE 17.—Typical elongated buboes of lymphogranuloma venereum. The enlargement of the nodes above and below the groin fold is characteristic.

FIGURE 18.—Ulceration of lymphogranuloma venereum of 15 months' duration.

the infection. In another the disease may manifest itself for years chronic residual lesions which may be so debilitating as to consign t patient to a life of invalidism. In one patient a single syndrome m undergo spontaneous regression or prove progressive for months or yea In another patient, particularly the female, various syndromes may prese themselves simultaneously or successively so that it is not uncommon see an inguinal bubo with vulvar elephantiasis or telltale inguinal sca with esthiomene, urethral, and anorectal syndromes. The strictures m be so marked as to lead to intestinal obstruction. The ulcerative lesio of the penis (fig. 18) or vulva may be extensive and very obstina Extraordinary hypertrophy and bizarre elephantiasic manifestations a seen with great frequency in Negroes and seldom in white persons. Beni tegumentary neoplasia of the vulva in the Negress may be due to t peculiar fibroblastic diathesis of the race.

Malignant neoplasia of the anus or vulva may be a direct sequel lymphogranuloma venereum in persons who possess an epithelial integ ment that responds to persistent irritating chronic inflammatory process so that anaplasia and metaplasia readily follow (*10, 13, 23*). Malignanc as a sequel to the chronic irritating discharges, is met in lymphogranulon venereum with greater frequency than pure coincidence allows (fig. 19).

Diagnosis

1. Frei test.
2. Biopsy.
3. Autoinoculation.
4. Complement fixation test.
5. Inverted Frei test.

1. *Frei test.*—The most important test in routine diagnosis is the Fr test. The Frei test is a confirmatory test. In the original Frei te sterilized and diluted pus was used. Later, Frei antigen of mouse bra origin was employed. Today the most reliable and best standardiz preparations are antigens of infected yolk of chick embryos along wi control material from uninfected yolks (*49*). The Frei test is perform by injecting 0.1 cc. of the antigen intradermally in the forearm so that wheal is raised. In positive cases an inflammatory infiltration or nodu measuring at least 5–6 mm. in diameter with a surrounding zone erythema is present at the end of 48 or 72 hours. If the test is negati at this time it is necessary to examine the area at intervals for seve days, since delayed reactions occur occasionally. A small area of necro or the development of a bleb in the center of the nodule or indurat zone signifies a strongly positive reaction. If a negative reaction is o tained in a patient in whom a positive result was expected, the test shou be repeated, because even in the early stage of bubo formation the t may be negative. The control test reaction, when uninfected chick em bryo material is used, should measure not more than 3 mm. Twelve

FIGURE 19.—Malignancy as a sequel to lymphogranuloma venereum in a young Negro woman 22 years of age with a rectal stricture of 2 years' duration.

forty days and longer may elapse from the time of the primary lesion befo a positive Frei test is obtained. A positive test remains so for life, b if the patient becomes debilitated or moribund a state of anergy intervene and negative reactions are obtained. A positive test may be reversed patients with lymphogranuloma venereum who have received intensiv sulfonamide therapy early in the disease (*35*). Once the disease h become well established, or in chronic cases, the test is irreversible in spi of intensive therapy.

2. *Biopsy.*—Histopathologic study frequently proves useful in t diagnosis of lymphogranuloma venereum, particularly in doubtful case In the bubo form there are inflammatory and suppurative changes in t lymph nodes as well as the perilymphoid tissue. There is a polymorph granulomatous reaction; tiny foci of necrosis or micro-abscesses surrounde by macrophages with occasional giant cells are seen. In the elephantias forms there is a pronounced peritubular infiltration with plasma cells ar lymphocytes, accompanied by fibroblastic activity, dilated lymphatics ar in some cases with giant cells of the foreign body type (*23*). Occasio ally, foci of suppuration are noted similar to those seen in buboes. the benign neoplasias of lymphogranuloma venereum, biopsy is frequent necessary for diagnosis and to rule out malignancy. The histologic pictu of lymphogranuloma venereum is not necessarily specific but is suggestiv Tissue removed from an inguinal mass in a young male, 25 years of ag with the clinical diagnosis of Hodgkin's disease revealed on histolog study a picture suggestive of lymphogranuloma venereum. Frei tests we done which were strongly positive. In many ulcerative lesions of t genitals, groin, and perineum, biopsy offers a means of diagnosis, partic larly in the presence of positive serologic tests for syphilis and intrac taneous tests for chancroid and lymphogranuloma venereum.

3. *Autoinoculation.*—Autoinoculation of aspirated pus from a bubo lymphogranuloma venereum does not produce a local ulceration, while chancroid the autoinoculation of aspirated pus frequently does produ a typical chancroidal ulcer.

4. *Complement fixation test.*—A serologic complement fixation test wi antigen from lymphogranuloma venereum virus of chick embryo orig is now commercially available. Although this test is not generally vogue it is said to be a very sensitive test and of much value in ear diagnosis as well as to gage the efficacy of treatment or progress of t disease (*46*).

5. *Inverted Frei test.*—In certain instances a negative Frei test is ob tained even in the presence of a suppurative bubo. The pus aspirate from such a bubo may be made into an antigen and on injection int known cases of lymphogranuloma venereum will evoke a positive respons The inverted Frei test may be of value in selected instances (*20*).

Preparation of Frei Antigen From Bubo Pus

The fluctuant bubo is aspirated under sterile conditions, using a 16 gauge needle. The surface of the bubo is first prepared by shaving and cleansing with skin disinfectants such as alcohol and ether, or iodine. Patients with positive blood serologic tests for syphilis, positive chancroid skin test, or fistulization of the bubo should not be used. Spreads and routine cultures of the aspirated pus are made to rule out the presence of bacteria.

The pus is diluted with 4 parts of sterile normal saline solution as soon as possible after aspiration. The diluted material is immersed in a water bath of 58° to 60° C. for 2 hours and on the next day for 1 hour. Further tests for sterility by spread and culture are made. If all bacteriologic tests are negative, then 0.25 to 0.5 percent of phenol is added to the antigen as a preservative. Known patients with lymphogranuloma venereum, particularly persons with rectal stricture, are tested. Incontestable positive reactions must be obtained in persons with proved lymphogranuloma venereum and absolutely negative reactions in normal controls and in persons with allergy to chancroid.

Treatment

1. *Chemotherapy.*—Evidence is accumulating that the sulfonamides are of some value in the therapy of lymphogranuloma venereum, particularly in its acute phase as in acute bubo or systemic infections (*36, 62, 68, 70, 76*). They are of particular value in ulcerative processes, draining sinuses, in proctitis and colitis. Ulcerative processes frequently heal, sinuses cease draining, and rectal discharges abate. However, little effect is noted on the rectal stricture per se or on the elephantiasic vulvae. These chronic manifestations are residual and involutional processes that are not benefited by chemotherapy. In selected cases of ulcerative colitis and rectitis due to the virus of lymphogranuloma venereum, sulfaguanidine orally, and sulfasuxadine enemata have proved of some value.

2. *Aspiration.*—Fluctuant buboes should be aspirated, repeatedly if necessary, but never incised.

3. *Vaccinotherapy.*—a. Subcutaneous or intracutaneous injections. Satisfactory therapeutic results have been ascribed to the subcutaneous and intradermal administration of Frei antigen. Biweekly or weekly injections of ascending doses of antigen from 0.05 to 1 cc. or repeated injections of 0.1 to 0.2 cc. over a period of months have been advocated. Striking results are occasionally obtained (*4, 22, 77*).

b. Intravenous therapy. Ascending doses of Frei antigen (0.05 to 0.5 cc.) of mouse brain or pus origin administered at 4- to 7-day intervals may be given to evoke fever as well as focal reactions. To assure some beneficial results, chemotherapy should follow this form of therapy. It appears to be of some value in chronim recalcitrant lesions (*24, 41*).

c. Convalescent blood. Transfusions from donors with a past histo of lymphogranuloma venereum may prove of value. One white woma with ulcerative colitis and rectal stricture was greatly benefited by su transfusions and was ultimately cured when sulfonamide therapy w added.

d. Convalescent serum. Intramuscular injections of 5 cc. of conval cent serum at weekly intervals have been advocated.

4. *Surgery.*—Polypoid excrescences, pedunculated tumors, and elepha tiasic vulvae may be removed. Healing usually takes place quite readil In some cases recurrences of the ulceration have been observed sever years afterward. Excision of the matted gland is permissible and is ind cated when the inguinal mass remains chronically indurated for mont without signs of suppuration or regression. However, as a general pra tice, excision is to be deprecated because it may be followed by seve elephantiasis of the genitals.

5. *Management of rectal stricture.*—Symptoms of pain, rectal leuko rhea, and most of the complaints coincident to rectal stricture are great lessened by sulfonamide therapy. The stricture should be gently dilate manually at weekly intervals. Long and short wave diathermy has a favo able effect on the inflammatory process and allows the stenotic lumen undergo softening. When the rectal stricture is so stenosed as not to adm the index finger, dilatation under anesthesia or caudal block is necessar Under anesthesia the stenotic lumen may be gently forced by the exami ing finger and the fibrous tissue broken down by gentle manipulatio Hegar dilators may then be used to facilitate adequate dilatation. Manu dilatation of the stricture must be performed at weekly or fortnightly inte vals, otherwise return of the stenosis may take place. When strictures a beyond reach of the examining finger, then colostomy is a justifiab procedure.

Differential Diagnosis

1. *Syphilis.*—Needless to say, it is urgent that syphilis be ruled out befo a final diagnosis of chancroid, granuloma inguinale, or venereal lympho granuloma is made. The primary chancre may simulate the initial lesio of these diseases, and quite frequently the chancre occurs in combinatio with one of these infections. Darkfield examinations for Treponema pa lidum should be done, and blood serologic tests for syphilis should b repeated at frequent intervals for at least 6 months. Secondary lesio of syphilis may at times require differentiation from the multiple aut inoculable lesions of chancroid or inguinal granuloma.

2. *Gonorrhea.*—An intraurethral infection with the virus of lympho granuloma venereum must be distinguished from gonorrhea by the absen of the gonococcus. The Frei test may be negative during the acute pha of urethritis caused by the lymphogranuloma virus, but on repetition positive reaction is usually obtained.

3. *Herpes progenitalis.*—The lesions of herpes praeputialis or labialis are commonly multiple. They always begin as a group of vesicular lesions which break down to appear as superficial but circumscribed abrasions. They never spread. Usually a history of previous crops of vesicles can be obtained, which healed with or without medication. Inguinal adenitis may be present, and the nodes may reach the size of a large walnut.

4. *Fusospirochetosis.*—In primary fusospirochetosis the early lesions have a moist, pinkish, glazed appearance. When ulceration gets under way it is rapid and destructive. The spirillum and vibrio of Vincent may be demonstrated readily in spreads stained with Wright's stain or by dark-field examination. Primary fusospirochetosis may be responsible for an erosive and gangrenous balanitis and may resemble a phagedenic chancroidal infection. Genital lesions frequently become contaminated with fusospirochetes, and occasionally these saprophytic organisms play a role in the destructive or recalcitrant nature of the underlying infection whether it be chancroid, granuloma inguinale, or lymphogranuloma venereum. Fusospirochetes are not necessarily destroyed by intravenous arsphenamine therapy, intramuscular bismuth therapy, or by antimony compounds. These secondary invaders are best treated by topical applications of arsphenamines or by oxidizing agents such as sodium perborate or zinc peroxide. A mixture found to be very useful in the treatment of fusospirochetosis contains 7 to 10 percent of arsphenamine in equal parts of cod-liver oil and glycerine. Some analgesic may be added to this mixture when its application proves painful.

5. *Pyogenic granulation tissue.*—The exuberant granulation tissue of infected wounds commonly referred to as "proud flesh" may simulate the granulation tissue of granuloma inguinale. Pyogenic granulation tissue frequency harbors intra- and extracellular organisms that may offer some difficulty in differentiation from immature forms of the Donovan body.

6. *Malignancy.*—Destructive chancroid, chronic indurated ulcerative processes or hypertrophic growths of lymphogranuloma venereum, or recalcitrant lesions of granuloma inguinale may simulate malignancy. Histologically, granuloma inguinale has been mistaken for malignancy. On histopathologic study of biopsy tissue, the marginal epithelial reaction may be marked hypertrophy or acanthosis. The rete pegs become elongated and the resultant relationship so distorted that islands of keratinized epidermis are frequently found deep in the section. These give the appearance of epithelial pearl formation and may simulate early epithelioma.

7. *Benign tumors.*—Benign tegumentary neoplasia of the vulva may result in pedunculated growths which may be confused with fibroma of the vulva.

8. *Blastomycosis.*—Blastomycosis of the pudendal region has been observed and in a measure simulates granuloma inguinale. The piled up, grayish pink lesions should not offer much difficulty since the blastomyces are easily demonstrated in spreads or biopsy section.

9. *Elephantiasis.*—Elephantoid enlargement of the scrotum commonly occurs with infection by Filaria bancrofti. Scrotal elephantiasis occasionally occurs primarily in lymphogranuloma venereum and secondarily in granuloma inguinale. Acute elephantiasis of the labia, temporary in nature, occurs at times in gonorrhea, in herpes labialis, after trauma, and in toxemia of pregnancy. Chronic elephantiasis of the labia or penis occurs primarily in lymphogranuloma venereum and secondarily in granuloma inguinale and malignancy.

10. *Inguinal bubo.*—The inguinal masses found in chancroid, granuloma inguinale, or lymphogranuloma venereum may resemble one another or be simulated by the other venereal buboes such as the hard, rock-like bubo of syphilis or the unilocular abscess of the rare gonococcal bubo. Tularemia (*51*), Hodgkin's disease, Pott's abscess or secondary malignancy of the inguinal glands, and nonvenereal regional adenitis must be thought of in the differential diagnosis.

11. *Anorectal disease.*—Anal carcinoma may be mistaken for the lobulated anal growths of lymphogranuloma venereum and vice versa. Rectal polyposis, gonococcal proctitis, and rectal carcinoma must be considered in the differential diagnosis of the various rectal manifestations of lymphogranuloma venereum.

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FOREWORD

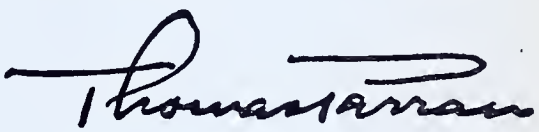
The National Conference on Postwar Venereal Disease Control may prove to have particular significance for medical and public health historians.

The new drugs and new methods of using older drugs, and the new emphasis on case finding may eventually be credited with the eradication of venereal disease as a major health problem in the United States.

Participation in the conference by physicians representing several of the Allied Nations may prove the first step in the development of practical methods for international venereal disease control.

Finally, future students may discover that the St. Louis conference marked the beginning of a broadened concept of the part to be played by ethical, educational, welfare, and law enforcement agencies in the *prevention* of infection.

Veteran leaders in the control movement observed another characteristic. They felt that this meeting of nearly a thousand physicians, laboratory scientists, nurses, administrative experts, educators, and social hygienists was marked by an undefinable sense of brotherhood in what might almost be termed a crusade. Certainly there was tangible sense of power, of great forces being set in motion toward a goal which now seemed far less remote than in previous meetings. There was less indecision, more unity, more determination, and more hope. Perhaps we who participated sensed that here was the briefing before the last, victorious drive against two ancient and stubborn enemies.



THURSDAY MORNING SESSION

November 9, 1944

The National Conference on Postwar Venereal Disease Control, under the auspices of the United States Public Health Service, Federal Security Agency, convened at the St. Louis Medical Society Building, at 10 o'clock, November 9, 1944. Dr. Thomas Parran, Surgeon General of the United States Public Health Service, presided.

The Chairman: This Third National Conference on Venereal Disease Control will come to order.

We have a message of greetings and regrets from the Governor of Missouri who finds it impossible to be here. The State Health Officer likewise is unable to be present. He is represented by a member of the State Board of Health, Dr. C. H. Neilson, who is also Assistant Dean of St. Louis University.

Dr. C. H. Neilson: Both Dr. James Stewart, Missouri State Health Commissioner, and Dr. Cleveland Shutt, President of the Missouri State Board of Health regret that they are unable to be present at this time and have delegated me, as Vice President of the State Board of Health, to welcome you on their behalf and for the Missouri State Board of Health. We all hope that you will have a good time and will be instructed and interested, as your work is so very timely.

The Chairman: We next are to have a word of greeting from Dr. J. F. Bredeck, the City Health Officer of St. Louis.

Dr. J. F. Bredeck: As the Health Commissioner of the city of St. Louis, we are very happy to welcome this meeting, because the problem that you have met here to discuss is one that is of very serious interest to us here in St. Louis. All of you know that when meetings of this type are held in any locality we always get an extra stimulus out of it in discussing our problems, and exchanging some of our difficulties. So in the name of the city of St. Louis I welcome you. I hope the meeting will prove successful, that you will renew many of your old acquaintances, and that you will leave with an increased interest in the vital subjects which will be discussed at this meeting.

The Chairman: Thank you, Dr. Bredeck. We are very deeply indebted to the St. Louis Medical Society for the opportunity of using this beautiful building and auditorium. We, therefore, are especially glad to have a word of welcome from Dr. Rogers Deakin, First Vice President of the St. Louis County Medical Association.

Dr. Rogers Deakin: I imagine that all vice presidents feel rather superfluous most of the time, but this is one occasion when I am glad that I am a Vice President of the St. Louis Medical Society, because it gives me the opportunity and the privilege of welcoming the members of this conference to St. Louis and to this building which is our home. I, personally, get a great deal of pleasure out of meeting so many old friends, and I am sure that all the members of the St. Louis Medical Society join with me in wishing you both a profitable and a pleasant meeting.

The Chairman: We expected to have the Honorable Watson Miller, Assistant Administrator of the Federal Security Agency, at this meeting but he seems to have been delayed.

The Honorable Paul V. McNutt, Administrator of the Federal Security Agency, has asked me to convey the following message to this National Venereal Disease Conference.

MESSAGE TO THE NATIONAL CONFERENCE ON POSTWAR VENEREAL DISEASE CONTROL

PAUL V. MCNUTT, *Administrator,*
Federal Security Agency

I deeply regret that unavoidable commitments prevent my meeting with you in this conference. My regret is tempered only by

my high confidence in those who have answered the call from all over the country and from other nations.

The sacrifice you have no doubt made in order to come here would be warranted only to consider a problem of inescapable national urgency. Venereal disease control is such a problem—a challenge where we can afford no relaxing of vigilance, where we must take prompt advantage of all the new weapons science has or can put into our hands.

I need not urge upon this meeting the serious, indeed, shameful, hazard which the venereal diseases still constitute to the health of the American people, in wartime and all the time. But I can reenforce this conviction with the first-hand knowledge which comes to me both from the Public Health Service and from other units of the Federal Security Agency, and from the War Manpower Commission. Our experience in marshalling the Nation's manpower for war has furnished additional proof that venereal disease is a specific handicap to all-out mobilization. This drain is measured not only in the terms of thousands of men unfit for military services, or unable to stand up under the heavy demands of war jobs. It is measured also by time lost from active duty within the ranks of our armed forces. It is measured again in the added burdens placed upon the Nation's desperately short medical, nursing and hospital resources. But even this is not all. To the physical havoc wrought by these diseases and by the conditions in which they breed must be added the social wreckage of twisted moral and ethical values, of warped and irreparably damaged lives.

For those of you who are medical men, health is the first responsibility. But I know you share our concern for other sectors in this complex and far-flung battle line. The Federal Security Agency has responsibilities not only for health but also for prevention and rehabilitation through constructive law enforcement, social welfare services, cooperation of business and community groups, and support of an informed and alert public. These varied approaches give us an opportunity to see the problem in broad perspective and to aid in building a united attack upon it.

This all-out attack is the more urgent because of our neglect following the first World War. During those years, Federal, State, and local appropriations for venereal disease control were practically nonexistent. There were hardly more than 500 public clinics, and most of them were in the big cities of the East. For that neglect we have paid in wasted manpower and in wrecked lives. But the price might have been even higher if it were not for the work of the last 8 years. With funds made available under the Social Security Act in 1936 and augmented under the LaFollette-Bulwinkle Act in 1938, the Nation-wide venereal disease control program has made great strides toward repairing the earlier damage.

This and other magnificent health advances since the turn of the century would have been impossible without the tireless vigilance of doctors and the cooperation of city, county, State, and Federal governments in mobilizing public health resources. Without the science and skill of modern medicine, without the teamwork of your profession, typhoid, cholera, yellow fever, diphtheria, and smallpox could not have been controlled; with your science, skill, and teamwork they have been brought—and kept—to a manage-

able minimum. Reducing syphilis and gonorrhea to a comparably manageable minimum is, as I understand it, your goal. To attain this demands even closer teamwork than against any other disease.

It needs continuation and progress in the strong government cooperation of recent years. Adequate appropriations and supporting legislation are essential to prevent another postwar shrinkage in official programs and facilities for case finding, diagnosis, and treatment. It also requires continuation of the good work being done by police and courts, and by social welfare and character-building agencies, in repressing prostitution and combatting social conditions leading to prostitution and promiscuity. Our experience in the Federal Security Agency, through the work of the Social Protection Division as well as the Public Health Service, has demonstrated the importance of these community services and of all-around community support.

If the Nation is to stamp out these diseases, the fight must enlist the organized help of our homes, our churches, our schools, and all our civic organizations. These are the guides to whom our young people look for counsel in weighing the values of life. This guidance is the very core of our American tradition, a tradition which our war experience has reenforced.

All the work and sacrifice that have gone and will go into the winning of the war are to the end that the world may be a better place in which to live. Here at this conference you are making a far-reaching contribution to victory and to the purposes of peace to which we are all dedicated.

ADDRESS OF WELCOME AND STATEMENT OF GENERAL PURPOSE OF CONFERENCE

THOMAS PARRAN, *Surgeon General,*
United States Public Health Service

This is the Third National Venereal Disease Control Conference sponsored by the United States Public Health Service. The first was called at Washington in 1936 to consider the principles which should underlie a national plan for the control of syphilis and gonorrhea. Out of that first conference grew a basic set of principles and a national platform of action for diagnosis, treatment, and control, which resulted eventually in the Venereal Disease Control Act of 1938. Under this act and the continuing appropriations made by the Congress from year to year has grown today's effective national network of clinics, laboratories, rapid treatment centers, epidemiologic and educational efforts. At that first national conference, Federal, State and local health departments and the medical profession were unified into one great team, a team backed strongly by public opinion.

The second conference was held at Hot Springs, Arkansas, in 1942, for the purpose of adjusting and broadening the national control program to meet the emergency of war. There was emphasis upon the need for tying together military and civilian efforts, not only on the medical side but for social protection and education as well. At the Hot Springs meeting I pointed out that the war has presented us with magnificent opportunities as well as diffi-

culties. Never before has a whole army been mobilized, the members of which have had serologic tests as a routine part of the physical examination. The Navy has followed the same plan. Never before has such a large number of our young men in military service been indoctrinated concerning the facts of the venereal diseases and their prevention. Never before have serologic tests been so widely used in connection with industrial employment, marriage and pregnancy, and never before have communities so generally undertaken to repress their commercialized prostitution.

During the past 2 years the revolutionary scientific tools which have come to hand represent our greatest and, as of 2 years ago, unanticipated opportunity. Science has evolved a treatment or system of treatment which is effective, rapid, and safe. Underlying this whole program and buttressing it we have seen an intensified educational campaign throughout the country. The net result of this has been that, after 3 years of war and more than 4 years of war and preparation for war, there are no signs pointing to any over-all increase in the attack rate of syphilis or gonorrhea in the general population. This reverses the history of any nation in any previous war. But we are not satisfied by defensive tactics or with merely holding our own against the venereal infections. As war progresses toward victory, plans must be laid for the critical period of demobilization and for the longer range postwar task.

Unless we begin now to make our plans, our Nation will be found unprepared on this important front during the very critical period of our national history. This conference therefore will not map a strategy of defense but rather a vigorous offense for the postwar eradication rather than control of syphilis and gonorrhea.

The period of demobilization will bring difficulties and also opportunities no less than did the period of mobilization. To check the venereal disease status of every member of the armed forces prior to discharge and to insure the necessary treatment for every one who has been found infected is itself a substantial task. Plans for this have been drawn and are already in operation. They were developed jointly by the military personnel and ourselves, with the approval of the Secretary of War, more than a year ago. Up to now more than 1,000,000 men have been discharged from the military forces. Let us consider what this means in terms of aiding in the control of the venereal diseases.

We have, in the armed forces, a group totaling perhaps 12 or possibly 13 million persons. As they go back to civilian life they go back clean or, in a small percentage, with their infection identified and they will be followed until cured. This means that among the most susceptible age group of the population we shall have a substantial number of clean, uninfected persons, representing what one might call a sanitary oasis in connection with this whole problem.

The period of demobilization after victory will bring new wartime problems, new problems, or old wartime problems in reverse. We can expect a further great shift in the population, and such shifts in themselves tend to increase infection rates. Of more importance will be the tendency to relax following our great wartime effort; this may be merely a negative phenomenon. There may be less public interest, less public concern, less public action on this

and other problems confronting the Nation, and it may be accompanied by lowered moral standards in sexual and other spheres. Whatever the actual form, it is clear that we shall have lost the motivation of patriotism, the drive for victory, inherent in the psychology of a people at war.

As a part of the problem confronting this third conference will be the prospective great expansion of travel and commerce between nations after the war. This will create greater opportunities for the spread of communicable diseases, including the venereal diseases. In the war theaters, international cooperation for the venereal disease control already has become well established. The presence here in St. Louis of so many distinguished medical officers from other United Nations makes it pertinent to discuss some of the bases for international action in this sphere.

In this connection I would recall to you the Brussels agreement of 1924, under the provisions of which a considerable number of the nations agreed to provide free treatment to mariners of other nations, that is, to merchant seaman at all principal ports of call. A broadening and strengthening of this agreement obviously will merit consideration as a part of postwar international measures for disease control. We shall be concerned here also with the effectiveness of new therapies, especially the more rapid treatment procedures, and of new drugs particularly the promise of penicillin, which drug happens to be effective against such diverse organisms as the Treponema pallidum and the Neisseria gonorrhoeae.

We shall further perfect our epidemiologic methods. In this connection we are encouraged to believe that much more can be done to get cases early under treatment by intensifying these methods. In fact, in our rapid treatment centers during the past 6 months there has been an increase of some 350 percent in the cases of early, that is, primary and secondary syphilis, and we are barely getting started in this effort to locate cases early and bring them under treatment.

We shall be planning hospital beds for the treatment of syphilis and gonorrhea in these rapid treatment centers. Also we shall be planning for their integration into the general hospital system of the country, with a view to their utilization in the care of other illnesses when we shall no longer need them for syphilis and gonorrhea. In other words, we are not planning a permanent complement of beds for these controllable diseases. For some of you younger men, especially my own staff who are engaged in venereal disease control, I anticipate that you will have worked yourselves out of a job before your professional career is ended.

At this conference, too, we shall review our present status and our future program for the repression of prostitution, for the prevention of sex delinquency, and for other measures of social protection and education. I am confident that we shall reaffirm our national policy for a vigorous repression of prostitution. Regulation of prostitution is objectionable because it fails. No system has been devised that will be obeyed either by those who profit from prostitution or by the women themselves.

One of my colleagues, Dr. LeRoy Burney, has just returned from visiting all of our major ports in Africa and Europe, the ports

which are being used by our merchant as well as military shipping. He says that the only suggestion that he could find in favor of commercialized prostitution was a statement of a port health officer, not an American, in one of the European ports. This officer said that his investigations had shown that only 60 percent of the women in houses of prostitution were infected while 70 percent of the other promiscuous women who were examined were infected.

Another colleague just returned from the fighting front reports that our commanders in the field are convinced that prostitution must be vigorously repressed. They are convinced, after trying other methods from time to time, that no other system works, and houses of prostitution are now out of bounds for American troops. I am sure, therefore, that all of us, certainly all of us in the Public Health Service, will continue to give the strongest possible support to the Division of Social Protection and to the other agencies concerned with the repression of prostitution.

The rapidity with which patients can be cured of gonorrhea by penicillin does not change our basic approach to the problem of prostitution. It was, I believe, about 15 years ago that the late Dr. George Bigelow raised the then hypothetical question as to what would be the policy in this country with respect to commercialized prostitution if we had an effective measure of immunization against both syphilis and gonorrhea and could immunize the whole population. I think that as health officers, and certainly as citizens, our attitude toward the accompanying evils of commercialized prostitution would cause us to continue our efforts for its repression.

I hope that the public health forces of this country will not take a narrow view concerning our part in this whole task. Not only are we concerned about treatment and epidemiology but, as I have indicated, we are concerned with minimizing the risks of infection, and with preventing contact with the disease by all measures at our command.

In the field of rehabilitation our job is not done if we bring in the infected spreaders of the disease, cure them within a day or two, or a week or two, and turn them back to the community, again to be reinfected. Such a policy is like shoveling smoke, turning the same thing over and over again. Therefore, I hope the public health forces here represented will take a broad view of all the factors which have to do with the spread of venereal disease and will lend their efforts wherever necessary.

Our rapid methods of treatment, too, do not change the necessity for strict enforcement of quarantine laws. Recent Federal legislation has given authority to the Public Health Service to deal with this problem in wartime, to invoke the powers of the Federal Government in imposing quarantine upon persons who travel interstate, upon persons who may infect war workers, who in turn may travel interstate, or persons who may infect military forces anywhere. I hope it will not be necessary to invoke these Federal quarantine laws, because ample authority resides in each State to deal with the problem on a State basis.

I have referred briefly to education. This conference will underline, I anticipate, the principles by which we have been guided from the beginning regarding the need for public education and which

must be intensified by the use of all appropriate material and all the media of public information. In short, I look upon this gathering as one of the most significant health conferences of our time.

I have spoken with confidence, perhaps with cautious optimism, during the past 10 years of our ability to control and even to eradicate venereal diseases. This confidence is strengthened by the course of recent discoveries in the field of chemotherapy. I have said that in spite of wartime there has been apparently no increase in this country in the attack rate of venereal diseases. There are some signs that indicate a reduction both in syphilis and in gonorrhea.

It is true that until recently we have not been able to bring under treatment any considerable proportion of the cases of gonorrhea, but we now are seeing significant increases in the number of cases which are coming for treatment. As regards syphilis, it appears that we are getting under treatment during the first year of the disease possibly one-half of the total number of syphilis cases which occur. It is because of the need of getting more of these cases and getting them earlier that I have emphasized, and I hope this conference will emphasize, the importance of being more thorough, of developing more intense methods for the discovery of cases in the very early stages. I refer to the gratifying increase in admission of primary and secondary syphilis to our treatment centers. Here we have a method of holding patients, of keeping them under treatment until they are cured, if we once can get at them before they have widely spread the disease.

With only a relatively slight increase in our total effort, by doing a more thorough job in some of the lagging communities, by putting the pressure where the diseases are the most prevalent, by leveling up the efficiency of our performance, it should be possible to discover a larger portion of the remaining new cases as they occur, those cases which at present are undetected.

It is a pleasure to welcome to this conference such a large group of distinguished, outstanding experts, who have come to share their scientific knowledge and ability with us. We count on you to plan both the strategy and the tactics for the task ahead. This task, I repeat, is to eradicate the venereal diseases as a public health problem in the United States. I feel that this is a historic task to which we have set our minds, our hearts, and our hands. Our Nation has a great destiny to fulfill. We workers in public health have a great contribution to make toward our Nation's future, in promoting the health and strength of our people.

The Chairman: The next address will be given by Dr. J. R. Heller, Jr., Chief of the Venereal Disease Division, United States Public Health Service.

PROBLEMS IN VENEREAL DISEASE CONTROL OF TOMORROW

J. R. Heller, Jr., *Medical Director*
Chief, Venereal Disease Division,
United States Public Health Service

The National Conference on Postwar Venereal Disease Control will not be defensive. We are preparing to attack. The sole motive

for this meeting is to establish additional means for drastically reducing the incidence of venereal diseases. As typhoid and smallpox have become unimportant diseases in this country because of unremitting diligence on the part of physicians and health departments, so must venereal disease be relegated to a minor role. Plans for the future must consider not only methods for lowering incidence but also for the maintenance of such ceaseless vigilance that never again will our people be burdened with syphilis and gonorrhea.

During the past few years remarkable advances have been made in treatment of syphilis and gonorrhea. These advances have been so far largely on a research basis. The principal agencies directing this research are the National Research Council, the Army and the Navy Medical Departments, and the United States Public Health Service. Preliminary reports have been very encouraging. The later reports which are to be made during this conference may confirm the belief that the physician at last has drugs and procedures adequate to solve the treatment problem. However, no matter how effective they are, these new drugs or new methods of administering old drugs can have little value for reduction of the attack rate of venereal diseases unless persons who are infectious are brought to the physician before they have spread their infections to others.

The most desirable, the most effective, and the least expensive approach to venereal disease control is through prevention. A first step in prevention is to find and immediately quarantine individuals with syphilis or gonorrhea before infection can be spread to others. Treatment is the most effective quarantine, since forcible separation of all infected persons from society is a procedure obviously impractical in this country. Prevention through personal prophylaxis, higher moral standards, prostitute repression, and education are all essential, but they are and always will remain secondary to treatment.

Our direct responsibility as physicians and health officers is for medical control measures and for dissemination of information about these diseases and their treatment. We recognize the need for and give our support to those programs which are intended to reduce prostitution and provide social welfare services, but their actual operation belongs elsewhere.

It is the tradition of physicians and other scientists to search everlastingly for the truth about the ills which plague mankind, and to make that knowledge available to other physicians and to the public. The obligation of physicians and health officers to tell the people the whole truth about venereal disease is as important as with any other communicable disease or hazard to health which requires individual and group cooperation from the general public. The people must know how syphilis and gonorrhea are spread. They must learn how venereal disease may be avoided and cured. Negative action which serves to keep these facts from the public serves to negate human progress. To tell the people the truth is to reaffirm our belief that when free and intelligent men and women are given the facts, they are capable of properly fashioning their destinies. To tell the scientific truth is to provide the strongest reinforcement to the church, to the home, and to the school in

their efforts to develop higher standards of sex conduct among all people. The broad dissemination of medical truth about venereal disease is essential if law enforcement and social agencies are to receive full public cooperation.

Venereal disease control of the future, so far as the physician and health officers are concerned, must devote a great deal more emphasis to case finding and to public education.

It is estimated that about 230,000 new cases of syphilis are being contracted in this country annually. Under existing methods and facilities for case finding we believe that each year only about three-fourths of these infectious cases are discovered and treated by public clinics, by the armed services, and by private physicians. We believe further that less than one-half of those found and treated remain under treatment long enough to insure against infectious relapse.

The unfound and untreated one-fourth and the insufficiently treated, lapsed cases are the source of infection for the annually recurring new crop of primary syphilis, and they accumulate year in and year out to form the great reservoir of latent and late syphilis.

There is no way of estimating with even reasonable accuracy the incidence of gonorrhea. Let us, however, take the arbitrary minimum ratio of 3 to 1 between gonorrhea and syphilis and assume that nearly a million people contract gonorrhea in this country each year—and this, may I remind you, is the minimum. During the past year private physicians and public clinics reported only 311,795 gonorrheal infections. For purposes of this discussion it is assumed that all of these reported cases received adequate treatment. There must be an extremely large residue of infected persons, therefore, who either receive no treatment at all or who resort to self-treatment. These are the people who keep the chains of gonorrheal infection going. These are the people who must be found and treated.

At present there are in the Nation's 3,800 clinics less than 2,000 workers engaged full time in investigating venereal disease contacts reported by the armed services, private physicians, and clinic patients. Additionally, about 6,000 health department nurses and social workers devote part of their time to venereal disease follow-up. These efforts do not suffice to perform the case finding which is necessary in the control program of the future. A few clinics are doing very fine contact investigation work. The majority are evidently making but slight effort to obtain the names and to locate the contacts of known infectious cases. Unfortunately, in many clinics vastly more time is given to holding old, noninfectious cases than in finding those which are spreading disease throughout the community.

The Public Health Service and most State health departments believe that vast improvement must be made in contact investigation before attack rates can be significantly reduced. Further, we believe that the extent of the problem requires that a great many more interviewers and investigators be recruited, trained, and put to work on orderly, well supervised case-finding programs.

In cooperation with State health departments and voluntary agencies, the Public Health Service is conducting research investi-

gations aimed at evolving the most successful methods of interviewing and contact investigation. It is reasonable to expect that these studies may form the basis upon which a well-rounded training program can be established.

During this war period one of the major factors in preventing a serious increase in venereal disease has been the information gained from the Selective Service examinations for syphilis, and from the contact reports furnished by the armed services to health departments. Within the past few months Selective Service has more or less ceased to be an active case-finding device, and as more soldiers and sailors are moved overseas, reports of their contacts in this country will begin to decline. When the war is over new case-finding procedures will be needed. This need will be intensified by sociologic, psychologic, and economic problems of readjustment which will probably be such as to cause a venereal disease problem no less acute than that caused by war itself.

Universal compulsory examination is not possible at the present time, so we must search for practical alternatives. Some of the opportunities for serologic and clinical examination for venereal disease which have been suggested and, at least, merit consideration by health officers and by private physicians include:

15,000,000 annual hospital admissions
1,500,000 annual marriages
2,500,000 annual births
1,500,000 annual high school graduations
370,000 annual college admissions
185,000 annual college graduations
4,000,000 annual insurance examinations
Several million industrial employment medical examinations.

Obviously, these are rough estimates containing vast duplication. It is apparent, however, that here are situations where medical examinations are or can be conducted and through which literally millions of opportunities for routine serologic and clinical examinations for venereal disease control can be obtained.

These are but a few of the problems and opportunities of venereal disease control today, and in the postwar period of tomorrow. In planning this conference it was felt that these problems and other aspects of venereal disease control could be grouped in four major classifications. Consequently sections were established for each category as follows:

1. Diagnostic and Therapeutic Procedures in Gonorrhea—Chairman, Dr. Rogers Deakin; Secretary, Senior Surgeon C. J. Van Slyke.

2. Diagnostic and Therapeutic Procedures in Syphilis—Chairman, Dr. A. W. Neilson; Secretary, Surgeon Howard P. Steiger.

3. Epidemiology—Chairman, Dr. N. A. Nelson; Secretary, Lt. Col. Robert Dyar.

4. Education and Community Action—Chairman, Dr. William F. Snow; Secretary, Dr. H. H. Hazen.

To these sections I give the following charges:

1. Section on Diagnosis and Therapy of Gonorrhea.—There never have been any reliable figures on the prevalence or incidence of gonorrhea in this country. The most conservative estimate is that

the attack rate of gonorrhea among soldiers and sailors is at least three times higher than that of syphilis. Many qualified observers believe that this estimate is too low for the general population. Whatever the actual incidence of gonorrhea, we know there is enough infection to make this disease a serious public health problem. We know also that not enough attention has been paid to the public health control of this disease. We know that our present knowledge of gonorrhea is inadequate. Conflicting theories regarding prevention, diagnosis, and treatment beset us from all sides.

It will be the responsibility, therefore, of the section considering diagnosis and treatment of gonorrhea to recommend means to bring system and order out of confusion and conflict. This section will examine all the evidence and, in terms of practical control measures, recommend as nearly as possible precise and definite procedures which may be followed by all official health agencies and through which the essential cooperation of the private physician may be insured.

The section will have to consider many questions. In the field of prevention it will need to review the possibility of developing more satisfactory prophylactic agents. In addition to those external agents which may be applied without irritation, the possibility of a systemic approach must be considered, such as oral administration of penicillin-like compounds or some immunizing vaccination procedure.

An important preventive topic is how physicians may better utilize their professional prestige in encouraging moral prophylaxis among their patients. Methods should be considered also for convincing both private practitioners and clinics of the supreme importance of obtaining from their patients information about contacts.

In this connection it is important to consider how the private physician can make effective use of the health department nurse as his personal agent in following up the infectious contacts of his patients. Better cooperation is also needed from the private physician in reporting cases of gonorrhea coming to his attention.

Many very complex problems will face this committee in the field of diagnosis. What are satisfactory diagnostic criteria? Will clinical and epidemiologic evidence suffice? Or must the physician also have laboratory evidence? These are important questions, as are the problems of whether positive spreads alone are sufficient evidence Further, we need to know if there is any difference between the reliability of spreads in male and female patients, and whether there is any difference between male and female with respect to acuteness and chronicity of the disease.

Many think cultures are essential in diagnosis. If so, should they be accepted only with carbohydrate fermentation tests?

Is sufficient recognition being given to nonpathogenic gonococcus-like organisms which may inhabit the genitourinary tract? In this connection, the possibility of confusion is illustrated by a recent study of 293 males selected more or less at random from a prison population. Of this group, gonococci were found in 3 men, while other Neisserian forms were found in 22.

The possibility of developing still other tests may be discussed,

complement fixation, for example, or an effective skin test. Many physicians are also interested in the development of more satisfactory methods for differential diagnosis of gonorrheal arthritis.

Gonorrhea therapy today is in a state of flux. It is difficult even to think about, much less to discuss anything other than penicillin. It is important, therefore, to bear in mind that the final time-dosage relationships have not yet been established. Any present method of therapy must give way promptly to improved schedules, methods, and treatment agents, antibiotic or otherwise, as soon as these have proved their worth.

What safeguards will this section recommend against the masking of syphilis by treatment of gonorrhea with agents which may prevent development of syphilis symptoms and yet are inadequate to arrest the disease? Assuming that penicillin or a similar effective and innocuous drug becomes available in sufficient quantity and at a reasonable cost, health officers will welcome this section's views as to whether it should be distributed freely to all physicians for treatment of their gonorrhea patients. Will it be advisable for the physician to use this free penicillin for gonorrhea treatment on the basis of any possible diagnosis or should he withhold treatment until diagnosis has been confirmed beyond reasonable doubt? These questions may be of paramount importance very soon.

The whole field of treatment of gonorrheal complications needs to be surveyed by this section, and, finally, the section will wish to include in its deliberations the question of criteria of cure.

2. Section on Diagnosis and Treatment of Syphilis.—It will be your duty and responsibility to weigh with utmost care the available evidence on new treatment drugs and methods and to decide which are to be recommended for use by the physician in private practice and for use in clinics and hospitals.

It will be your duty to recommend in general terms how the drugs are to be distributed and utilized so that treatment will be available to every person with syphilis in this Nation regardless of economic status, race, age, or place of residence. This must be done with the least possible disturbance to the traditional relationships between the private physician and his patient, and between Federal, State, and local health departments in their accepted spheres of public responsibility.

If you believe that further research and observation are necessary before general use of the new drugs and treatment methods can be urged, you should make specific recommendations.

Equally important in your deliberations will be the question of diagnosis of syphilis. It is obvious that successful new treatment schemes are of limited value to public health unless infected persons are found early in the infectious stage and brought to an effective treatment source. It is of the utmost importance that we institute a program of case finding vastly larger in scope and effectiveness than now practiced. Consideration of the case-finding problem is the responsibility of the section on epidemiology, but diagnosis and case finding are closely related.

Large-scale case finding is handicapped so long as our major diagnostic technic for syphilis is regarded by the public as inconvenient. A radically improved test would solve many problems in

case finding. The test which we need should be fast, painless, specific, sensitive, and simple. It may be that this new test will be found only through the combined and coordinated effort of the best scientific minds in this Nation.

It will be the duty of this section to cite what resources of microbiology, immunology, biochemistry, organic analysis, physics, and other sciences must be called upon to develop a diagnostic test for syphilis comparable in speed and specificity to the new treatment methods. Previous investigations should be reexamined and extended if they suggest promising potentialities; new approaches should be sought and explored. The United States Public Health Service is prepared to sponsor and support research recommended to this end by the Section on Diagnosis and Treatment of Syphilis.

3. Section on Epidemiology.—Contact investigation theoretically offers the most direct approach to breaking chains of infection and reducing the incidence of venereal disease. I should like to review the contact investigation process and to consider its present status as exemplified in a group of 6 States for which complete data are available.

Interviewing is the first requisite of contact investigation. Follow-up workers cannot locate infected contacts unless they are first reported by treatment sources. Table 1 gives ratios of contacts reported per new admission for previously untreated cases of primary and secondary syphilis during two 6-month periods in 6 areas. The ratios include familial as well as nonfamilial contacts. You will note that the ratios vary greatly from area to area. In area Number 3 there was a substantial increase in the ratios from one semiannual period to the other. Increases were registered in 3 other areas also, with 1 area showing a decrease.

Contact investigation has been emphasized in the venereal disease control programs of all 6 areas, and the reduction in the contact ratios in 1 area suggests that continued vigilance is necessary to maintain a program even at a moderately productive level.

The contact investigation process is not an easy one. It is not only necessary to produce a volume of contact reporting, it is also necessary that adequate information be obtained in order that follow-up workers may locate contacts and bring them in for examinations. In table 2 the contacts reported have been divided into two groups, those with complete name and address and those with less information. As is to be expected, a much higher percentage of cases with a complete name and address are located than other cases; however, it is significant that it is possible to locate contacts even though a complete name and address is not given. Altogether it is seen that approximately half of the named contacts are located. Medical intelligence is of inestimable value in this procedure.

Locating named contacts in itself, however, does not reduce the spread of infection. It is only by bringing newly discovered infectious cases under treatment that the chain of infection can be broken. Table 3 shows the ratio of new infections brought to treatment for the first time to the patients by whom they were reported. In the best area for which tabulations are available approximately 30 new infections have been located as the result of investigating contacts of 100 new admissions to treatment with primary and

TABLE 1.—*Contacts reported per untreated admissions for early syphilis and gonorrhea by diagnosis of informant. Selected areas*

July through December 1943 and January through June 1944

Diagnosis of informant	Area	Clinic admissions		Contacts reported		Contacts reported per clinic admissions	
		July–December 1943	January–June 1944	July–December 1943	January–June 1944	July–December 1943	January–June 1944
Primary and secondary syphilis	I	380	366	417	471	1.10	1.29
	II	346	324	361	334	1.04	1.03
	III	512	435	241	510	0.47	1.17
	IV	354	362	960	1233	2.71	3.41
	V	119	212	225	311	1.89	1.47
	VI	194	256	246	454	1.26	1.77
Early latent syphilis	I	594	448	437	439	0.80	0.98
	II	1395	863	1545	1127	1.11	1.31
	III	3004	2099	623	1380	0.21	0.66
	IV	480	553	533	863	1.11	1.56
	V	420	431	340	194	0.80	0.45
	VI	387	417	312	564	0.80	1.35
Gonorrhea	I	1510	1749	1072	1273	0.71	0.73
	II	3956	2614	1987	1890	0.50	0.72
	III	3052	2675	1037	1290	0.34	0.48
	IV	3006	2999	2944	3306	0.98	1.10
	V						
	VI	1432	2005	953	1838	0.66	0.92

secondary syphilis. This is an underestimate to the extent that outside health jurisdictions, including the armed forces, may have failed to report results of investigations. The ratios for early latent syphilis and gonorrhea are much lower. Except in area Number 4, contact investigation with respect to gonorrhea has not been a very effective method of breaking the chains of infection. In considering the stages of syphilis, it will be noted that in the best area only 11 of the newly discovered cases are in the primary and secondary stages, and 8 are in unknown stages which may or may not have been primary and secondary stages. In the 5 other areas a greater proportion of the newly discovered cases are in the latent stage than in the open lesion stage.

Why is this? To the extent that contacts reported are source contacts, we should expect them to be in the latent stage upon discovery, especially if the investigation is unduly delayed; however, investigation on spread contacts should bring more results in terms of infectious syphilis. If in interviewing for contacts, efforts are confined to obtaining names of sources, contact investigation is analogous to "locking the barn door after the horse has been stolen." A venereal disease control program should attempt to stop the spread of infection. The location of spread contacts offers an opportunity to diagnose and render them noninfectious before there is time to pass on the infection.

I do not wish to imply that contact investigation of sources is not important, but it should be emphasized that investigation of possible spread contacts is, to say the least, equally important in

TABLE 2.—*Relation between completeness of information on nonfamilial contacts and percent located in 60 days by diagnosis of informant. Selected areas*

January through June 1944

Diagnosis of informant	Area	Complete name and address			Incomplete name or address			Total		
		Contacts reported[1]	Contacts located		Contacts reported[1]	Contacts located		Contacts reported[1]	Contacts located	
			Number	Percent		Number	Percent		Number	Percent
Primary and secondary syphilis	I	317	239	75.4	99	30	30.3	416	269	64.7
	II	110	59	53.6	107	46	43.0	217	105	48.4
	III	204	139	68.1	188	95	50.5	392	234	59.7
	IV	285	169	59.3	184	59	32.1	469	228	48.6
	V	100	61	61.0	53	13	24.5	153	74	48.4
	VI	198	139	70.2	103	49	47.6	301	188	62.5
Early latent syphilis	I	199	141	70.9	56	12	21.4	255	153	60.0
	II	249	169	67.9	256	98	38.3	505	267	52.9
	III	542	334	61.6	371	158	42.6	913	492	53.9
	IV	151	76	50.3	51	21	41.2	202	97	48.0
	V	44	30	68.2	14	2	14.3	58	32	55.2
	VI	252	153	60.7	86	39	45.3	338	192	56.8
Gonorrhea	I	940	757	80.5	251	86	34.3	1191	843	70.8
	II	912	611	67.0	717	258	36.0	1629	869	53.3
	III	821	566	68.9	425	223	52.5	1246	789	63.3
	IV	2070	1375	66.4	703	308	43.8	2773	1683	60.7
	V	731	543	74.3	210	53	25.2	941	596	63.3
	VI	1366	913	66.8	391	163	41.7	1757	1076	61.2

[1] Contacts known to be out of area excluded.

breaking the chain of infection. In fact, interviewers should attempt to identify all contacts from the date of interview back to the earliest probable date of infection with no arbitrary distinction between source and spread contacts.

Perhaps we are discouraged as we look at these accomplishments of the contact investigation program. These are not neglected areas, but rather ones in which contact investigation has been emphasized, at least for the past 2 years. That increased emphasis can produce results is demonstrated in area Number 3 where the ratio has increased within a year from 0.06 to 0.17. It should also be noted from these figures that the lower the ratio the lower the percentage discovered in the open lesion stages.

In table 1 a higher ratio of contacts per new patient is shown for the last 3 areas than for the first. In table 3, a higher ratio of new infections brought to treatment is shown for the last 3 areas than for the first 3. There is also a significantly higher proportion of contacts in the open lesion stages in the last 3 areas than in the first 3. Does this indicate that where the ratio of contacts reported is low, interviewing is more restricted to source contacts? As I have stated, these areas have relatively effective contact investigation programs, and it is doubtful if complete figures were available for other States that any great improvement would be shown.

If we conclude that these figures indicate the present status

TABLE 3.—*Contacts brought to treatment per untreated admission for early syphilis or gonorrhea and contacts brought to treatment, classified by presence of lesions, per untreated admission for early syphilis by diagnosis of informant—Selected areas*

July through December 1943 and January through June 1944

Diagnosis of informant	Area	Clinic admissions		Contacts brought to treatment		Contacts brought to treatment per new case		Contacts brought to treatment per new case (by lesions)		
								January–June 1944 syphilitic lesions		
		July–December 1943	January–June 1944	July–December 1943	January–June 1944	July–December 1943	January–June 1944	Present	Not present	Not specified
Primary and secondary syphilis	I	380	366	57	57	0.15	0.16	0.06	0.08	0.02
	II	346	324	43	42	.12	.13	.05	.08	.00
	III	512	435	31	76	.06	.17	.04	.12	.01
	IV	354	362	110	105	.31	.29	.11	.10	.08
	V	119	212	25	44	.21	.21	.09	.11	.01
	VI	194	256	37	62	.19	.24	.09	.11	.04
Early ilatent syphils	I	594	448	40	48	.07	.11	.02	.07	.02
	II	1395	863	153	69	.11	.08	.01	.07	.00
	III	3004	2099	57	146	.03	.07	.00	.06	.01
	IV	480	553	48	49	.10	.09	.00	.06	.03
	V	420	431	52	20	.12	.46	.00	.46	.00
	VI	387	417	27	63	.07	.15	.01	.11	.03
Gonorrhea	I	1510	1749	97	172	.06	.10	------	------	------
	II	3956	2614	253	186	.06	.07	------	------	------
	III	3052	2675	124	154	.04	.06	------	------	------
	IV	3006	2999	642	705	.21	.24	------	------	------
	V	------	------	------	------	------	------	------	------	------
	VI	1432	2005	151	239	.11	.12	------	------	------

of contact investigation in the United States, do they offer much hope of breaking the chains of infection? If continued at its present level, I believe the answer is no. Here is what can be done to improve contact investigation as a process which offers reasonable hope of a reduction in the incidence of venereal disease.

1. The volume of contact reporting must increase. This means more interviewing in clinics, hospitals, and rapid treatment centers. The ratios indicated are for complete health jurisdictions, such as State or city. The figures for individual clinics show a much greater range of variation. It is not merely a question of increasing the ratio in clinics in a State from 1 to 2 or from 2 to 3; it is a question of maintaining the higher level of the effective clinics and raising the level of the others.

2. The type of information must be improved. Large numbers of contact forms containing wholly inadequate information should not be offered to follow-up workers. Determined efforts should be made to improve the type of information by the introduction of an adequate form for recording the information. Attempting to record contact information in an utterly inadequate space on a patient's chart is not conducive to good interviewing.

3. We must determine to obtain the names and investigate persons to whom the patient may have given the infection, as well as the source. This does not mean that in interviewing source and

spread contacts should be defined, but rather that the names of all exposures from the date of interview back to the date of possible infection should be obtained.

4. The introduction of rapid treatment centers and the trend toward inpatient treatment offers a loophole, but a dangerous one, in the contact investigation process. When patients are not treated in the clinic making the diagnosis, there is a tendency for the clinic to assume that the treatment agency will interview the patient concerning contacts, and also for the treatment center to assume that the referring clinic has obtained the contact information. As a result the patient may not be interviewed at all.

Rapid treatment centers offer unique opportunities for carrying out not only the initial interviews but also the later ones. On the other hand, it is desirable for the diagnostic clinic to obtain immediately information regarding contacts. If referring clinics could forward to the treatment centers a summary of information regarding their contact interviewing—possibly by means of copies of actual contact reports prepared—the treatment agencies would be in a position to continue the interviewing in an intelligent fashion and without repetition.

Even with excellent interviewing and follow-up of contacts reported by patients in clinics, a large segment of the syphilis population remains untreated. Contact investigation at the clinic level may succeed in breaking numerous chains of infection, but some chains are never included in this process. To succeed in breaking a chain of infection, it must be recognized at some point. The patients of private physicians constitute links in chains usually not entered by contact investigation, which is initiated at the clinic level. What can be done to utilize the contact investigation process in breaking these chains of infection? I leave this problem to the ingenuity of the Epidemiology Section.

4. Section on Education and Community Action.—It will be the duty of this section to deal with the nonmedical community aspects of postwar venereal disease control. The impact of demobilization and reconstruction upon a people uprooted and weary of restraint may have very serious implications for the control program over the next several years.

We have based our appeal for the repression of prostitution upon a win-the-war psychology. What will be our substitute when the war is over and the inevitable reaction sets in, when the forces of commercialized vice come out of hiding and begin to revive their sordid activities?

Community action for venereal disease control involves such extremely important matters as prevention of delinquency, enlightened probation policies, facilities for wholesome recreation for young people, for redirection and social services. When the motivating stimulus of war need is removed, is it proper and necessary to urge governmental and voluntary agencies to continue their programs in these fields?

What will be your answer to those sincere people who believe that widespread dissemination through public channels of information about venereal disease and the teaching of social hygiene to school children encourage immorality and, therefore, defeat their purpose?

On the other hand, what will you say to those equally sincere people who believe that to withhold information about venereal disease from the general public and from young people in particular is itself an act of immorality? With respect to official health agencies, these same people contend that to fail to conduct public venereal disease education is to be guilty of dereliction of duty. What course of action, therefore, will you recommend to Federal, State, and local health departments and to voluntary agencies?

There is also the technical question of whether venereal disease education and social hygiene involve such specialized and complicated problems that they should be handled separately from generalized community health education. An expression from you will be welcomed by all health educators.

With the advent of shorter, safer, and less inconvenient treatment methods, how will we prevent our education from misleading the public to believe that promiscuity has been made safe and has thus received the blessing of science? In view of this possibility, would it be advisable to conduct simultaneously with public venereal disease education an equally intensive campaign of education for higher standards of sex behavior? If you feel this collateral effort is necessary, who should be responsible for its planning and execution? If you believe that official health agencies should actively participate in education for morality, is it possible that this would establish a dangerous precedent, possibly leading toward governmental interference with religious and family life?

The Public Health Service hopes that the chairmen, secretaries, and committees will serve as continuing committees after this conference, since it is realized that all the questions before the committees cannot possibly be answered in the brief time allotted. However, the Public Health Service hopes that out of these deliberations, out of the recommendations of this group through its component committees, there will come a pattern for venereal disease control that finally will bring the day when we can eradicate the venereal diseases.

The Chairman: The next address will be by Lieutenant Colonel Sternberg of the Army of the United States.

ARMY CONTRIBUTIONS TO POSTWAR VENEREAL DISEASE CONTROL PLANNING[1]

THOMAS H. STERNBERG, *Lieutenant Colonel,*
and
GRANVILLE W. LARIMORE, *Captain*
Medical Corps, Army of the United States

It is even now apparent that the approaching demobilization period will be accompanied by many serious problems in the control of the venereal diseases. During and following previous wars the incidence of venereal disease has always reached epidemic proportions. While the maintenance of low military rates during the first 3 years of the current conflict justifies a feeling of achievement by all concerned, it is noteworthy that since the first of January 1944, the Army venereal disease rate for the continental

[1] From the Venereal Disease Control Division, Preventive Medicine Service, Office of The Surgeon General, United States Army.

United States has risen steadily to a present level of 36 per 1,000 men per year, as compared to the 1943 rate of 26.3. Furthermore, it is our belief, based on the following considerations, that the Army rate in the continental United States will continue to rise for some time, and may even reach World War I levels.

1. It is increasingly evident that a general let-down in the overall venereal disease control program, both military and civilian, is in progress.

2. The outstanding advances in therapeutic methods climaxed by the introduction of penicillin have resulted in (a) better reporting of venereal disease with a decrease in the amount of concealed gonorrhea, (b) a definite but as yet unmeasured effect on the will of the soldier to avoid venereal disease, and (c) a reduction in the man-days lost per 1,000 men per year from 1,280 in 1940 to a current low record of less than 300, giving rise to a further loss of interest in prevention.

3. Due to overseas assignment, the group of young trained venereal disease control officers initially stationed in this country has been depleted to almost the vanishing point. While this has lowered the intensity of our venereal disease program at home, it is with a great deal of satisfaction that the downward trend of the venereal disease rates in all Theaters of Operations is recorded. The combined overseas rate for all American soldiers is now 25 percent lower than for those stationed in the United States.

4. Troops returning from overseas areas have had an abnormally high venereal disease rate of infection, acquired after arrival in this country. This is an increasingly serious problem. It can be explained in part by the effects of long overseas duty, and by the belief of these men that the girls in this country are free of infection.

It is obvious that these problems affect the civilian and military alike, and present a rather gloomy picture for the immediate future. Despite this, it is our opinion that in the postwar period there will exist an unprecedented opportunity to reduce the incidence of the venereal diseases to a manageable minimum. This opportunity, to be fully exploited, will require a critical evaluation of our current control measures with a view towards their strengthening and expansion, and a recognition of the changing aspects of venereal disease control brought about by more effective therapeutic weapons and by the mass wartime experience with educational and case-finding procedures.

It is believed that in the planning for postwar venereal disease control the Army has much to offer in the way of material assets and experiences. It is our intention in this paper to discuss specifically these contributions not only with respect to actual demobilization procedures but also in relation to the strictly civilian activities of venereal disease education, case finding, and community action.

DEMOBILIZATION PLANS

During the past 6 months the Army, in collaboration with the United States Public Health Service, has developed demobilization plans in respect to venereal disease which may be outlined as follows:

1. A physical examination for venereal disease and a routine serologic test for syphilis will be performed on all soldiers within the 48 hours prior to their discharge from the Army.

2. Retention and treatment of all soldiers with gonorrhea and chancroid, and of those with evidence of active syphilis, either early or late. These patients will be treated until cured, or in the case of syphilis they will receive a course of penicillin which is believed to be curative, but which in any event will render the individual noninfectious.

3. Referral to appropriate State health departments through the United States Public Health Service of (a) the name and civilian address of previously untreated soldiers found at the time of separation to have latent syphilis as evidenced by a positive serologic test, and (b) all pertinent information on soldiers under treatment or previously treated by the Army, provided further medical attention is considered necessary.

The application of this plan to over 7,000,000 soldiers will be of considerable value to the over-all civilian program in that it represents (1) a mass case-finding procedure, (2) a uniform method of transition of partially treated or incompletely observed cases from the Army to the civilian, (3) a mechanism for detecting the previously unidentified failures to the prescribed course of treatment, and (4) a method of obtaining a final evaluation of Army treatment schedules, both mapharsen-bismuth and penicillin.

In such a mass procedure, some errors are bound to occur. Some of the positive tests will upon investigation prove to be technical or biologic false positives and it is important that these individuals not be considered syphilitic until proven so by subsequent examination. Further, it is inevitable that an occasional case of infectious syphilis or gonorrhea will escape identification during the final physical examination, or will be in the incubation period at that time.

MEASUREMENT OF TRENDS

Unfortunately, our present methods of measuring incidence of infectious venereal disease in civilian populations, based on reported cases, are subject to so many errors that they are difficult to evaluate. On the other hand, the incidence rates for venereal disease in the Army reflect to a considerable degree the incidence of infectious venereal disease in the civilian community, and may therefore be used in determining trends in the civilian population.

While the total Army venereal disease rate in the continental United States has risen sharply since the first of January 1944, a breakdown by disease reveals the increase to be entirely due to gonorrhea. The epidemiologic picture in this disease is far from encouraging. The recent 40 percent increase in the Army gonorrhea rate must reflect, at least partially, an increase in the incidence of civilian gonorrhea. Since military data invariably show a ratio of 6 to 7 cases of gonorrhea to 1 of syphilis, it may be assumed that a similar ratio prevails in the civilian population. If this assumption is true it suggests that an enormous amount of unrecorded and presumably untreated gonorrhea exists in the civilian population, and indicates the relative inadequacy of our present gonorrhea control program.

However, during the past year the Army syphilis rate has declined 20 percent. It is hoped and believed that this decline is due to a lowering of the civilian reservoir of infectious syphilis brought about through the admittedly better case-finding technics in this disease, plus the effect of the rapid treatment programs.

POSTWAR PERSONNEL RESOURCES

These figures on the disproportionate decline in syphilis and increase in gonorrhea present encouraging evidence of success in the syphilis control program which should serve as a stimulation to even greater efforts towards the elimination of this disease. They also, of course, indicate the great need for the development of an effective gonorrhea control program. The accomplishment of these objectives will to a large extent depend on the availability and proper utilization of trained or experienced personnel. and the Army will contribute greatly to this task.

Availability of experienced physicians during demobilization.—During the war several thousand medical officers have received formal training or experience in the control of venereal disease and in general public health procedures. The majority of these officers were general practitioners in civilian life and will return to their offices when released. They should be encouraged to continue their interest in and support of venereal disease control as an aspect of preventive medicine. The role of the private practitioner in the control of the venereal diseases has been underemphasized. It is vital to the success of the over-all program that a better relationship between the health officer and physician be established to the end that every physician is either his own adequate epidemiologist or permits access to his patients of an accredited health department representative.

Utilization of Army lay venereal disease control officers.—A second contribution the Army will make to civilian postwar personnel resources will be several thousand enlisted men who have had extensive training and experience in the nontechnical aspects of venereal disease control procedures. Many of these have devoted most of their Army service to taking contact histories, and have become very proficient in this task; others, both white and Negro, have acted as noncommissioned venereal disease control officers with considerable distinction; more than a thousand are graduates of formal courses in venereal disease control for noncommissioned officers, given at several Army posts during the past 3 years. The value of male nonmedical contact follow-up personnel has been demonstrated in several State health departments as well as in the Army, and it is believed that health departments and clinics should consider the employment of these individuals as they are demobilized.

INFLUENCE OF TREATMENT ON CASE FINDING

An important factor that has had a marked influence on case finding in the Army has been the introduction of penicillin in the treatment of gonorrhea When penicillin was first made available to the Army for the treatment of this disease, many soldiers with successfully concealed infections voluntarily reported at sick call and asked for penicillin treatment. This experience would seem

to have considerable significance to civilian case-finding programs, indicating that at the proper time widespread publicity in respect to the availability of penicillin and its nontoxicity and effectiveness will result in many hidden sources of infection voluntarily seeking treatment.

POSTWAR COMMUNITY ACTION

During the past few years community organization and action towards the control of the venereal diseases, stimulated and assisted by the military, Federal, and voluntary agencies, has reached a peak of popular support and interest which will be difficult to maintain. As the end of the war approaches it is becoming increasingly evident that the danger of a serious let-down in these activities is imminent. Since in the postwar period Army support of community action will no longer have either the influence or authority as during the wartime period, it is believed urgent that all agencies and local groups concerned immediately direct their planning towards peacetime activities, justified on the basis of a permanent community need, rather than as a temporary aid to the Army in time of war.

Influence of Army personnel in postwar community programs.—In the Army, commanding officers of all grades are charged with the responsibility of maintaining health in their organizations, and by regulation they are, with the advice and assistance of the surgeon, specifically delegated the task of development and maintenance of venereal disease and preventive medicine control programs. The so-called command aspect of public health practice carries down through the noncommissioned officer to the enlisted man and the subject is included in all training courses. Thus demobilization will return to the communities hundreds of thousands of officers and millions of enlisted men who have had first hand knowledge of the principles of preventive medicine. Many of these men are the civic leaders of tomorrow and every effort should be exerted to assure their active participation and support in all phases of community action directed towards the control of venereal disease.

VENEREAL DISEASE EDUCATION

During the past few years the Army has enjoyed a unique experience in being able to apply, on a compulsory basis, intensive venereal disease educational procedures to large masses of men. This program, beginning at the time of the soldier's induction and carrying through to his discharge, is carried out by commanding officers, medical officers and chaplains, utilizing every accepted method of approach.

It is significant in terms of the over-all civilian educational program that the Army alone will have returned to civilian communities, by the end of demobilization, over 9,000,000 men who have been subjected to this instruction, a circumstance which will, we hope, raise the general venereal disease educational level of the Nation to a new high. With these men as a nucleus, an opportunity exists to remove forever the venereal diseases from the realm of the unmentionable.

Because of current publicity and conflicts over education as a

venereal disease preventive measure it seems desirable that the Army mass experience in this phase of venereal disease control be made available. The amount and variety of venereal disease education to which the average soldier is exposed is certainly larger and more concentrated in point of time than is currently applied to the civilian population. Further, it has been possible through observations of individual organizations to formulate opinions as to the value of various educational materials and methods of presentation. Some of these are here offered as being of possible significance in the planning of future civilian venereal disease educational programs.

First, it must be recognized that there are two distinct and separate phases of venereal disease education: (1) The imparting to the individual of adequate technical knowledge of the venereal diseases and their prevention, and (2) the motivation of the individual with the will to avoid either illicit sexual intercourse or unprotected sexual exposure. Much of the confusion as to the actual role of education and no small part of the criticism that has been leveled against it as a venereal disease preventive measure arise from a failure to consider these two aspects as separate entities.

It must be admitted that an individual cannot intelligently protect himself against venereal diseases if he does not know what the diseases are, how they are spread, and the correct methods of prevention, including continence. Yet it must also be accepted that the possession of merely technical knowledge is no assurance that it will be used when needed. We have seen not one but literally thousands of examples demonstrating that possession of mere technical knowledge of the venereal diseases is of limited value as a preventive measure and that to be effective, venereal disease educational procedures must also impart a motivation for the avoidance of venereal disease. This motivation involves complex, and in many instances intangible factors, which in the Army are related to such diverse conditions as the religious and educational background of the soldier, the influence of the home and community, the attitude of his commanding officer, the esprit de corps of his unit, fear of the diseases or their treatment, fear of shame or ridicule, and many others, over most of which the Army has little direct control.

The Army, through the Corps of Chaplains, and through venereal disease educational material has continuously stressed continence as the most desirable and satisfactory method of avoiding venereal disease. Yet the strictly moral approach has been of limited value. This is attributed, at least in part, to the fact that molding of character and establishment of standards of personal conduct should and must be accomplished by the home, church, and community at an early age. Because venereal disease is a biologic accident of the sex act, an effective moral program will prevent infection, but the imparting of proper standards of personal conduct to the individual is not venereal disease education in the sense in which we are using the term, and should not be so considered. Therefore, the role of the physician and health officer in venereal disease control programs is necessarily limited. He can assume responsibility for the dissemination of scientifically accu-

rate information, and for the provision of adequate treatment, prophylactic, and epidemiologic facilities. He can and should support and assist those educational programs designed to influence sex behavior; but he cannot be expected to assume primary responsibility for the development of moral integrity.

PROPHYLAXIS

In the Army there seems strong reason to believe that the condom has been the most valuable single venereal disease preventive measure, as evidenced by the extent of its utilization.

Chemical prophylaxis administered at a fixed station, on which great reliance has been placed in theory and in past practice, has been difficult to popularize in this emergency because of the frequent inaccessibility of stations, the time consumed in administering treatment, the messiness, occasional discomfort and lack of privacy. Early in 1943, in an effort to improve individual chemical prophylaxis, the Army, in collaboration with the Subcommittee on Venereal Diseases of the National Research Council set about to develop a single-tube chemical prophylactic, effective against syphilis, gonorrhea, and chancroid. After considerable experimentation, an ointment containing 15 percent sulfathiazole, 30 percent calomel, 40 percent petrolatum, 14 percent light mineral oil, and 1 percent cetyl alcohol was subjected to field trials at 6 Army posts, in lieu of the regular station prophylaxis. The instructions were simple and the entire procedure required only several minutes, was acceptable cosmetically, was unaccompanied by discomfort, and was easily self-administered. At all 6 of the trial stations the prophylactic rate doubled or tripled merely through the spread by word of mouth that the Army had a new and improved prophylactic. This material has now become a standard Army prophylactic item distributed under the name of Pro-Kit.

It would appear from this experience that one important reason for the failure of individual chemical prophylaxis to "take" in civilian life has been the unsatisfactory products available. Postwar venereal disease control planning will be incomplete without provisions to make this item freely available at a price commensurate with its cost of production.

VENEREAL DISEASE CONTROL IN NEGROES

The Negro venereal disease rate in the Army has consistently been higher than the white rate. Negro troops have received the basic venereal disease control program given to white troops, and additional specific measures have been directed from a national level. These have been ineffective in lowering the over-all Negro rate. However, successful Negro venereal disease control programs are possible on a local level, as demonstrated by the consistently low rates maintained at Tuskegee and several other posts where large numbers of Negroes are stationed. Several of these programs were organized and carried out by superior Negro medical officers, backed by strong command support, and utilizing all available control procedures, including suppression of prostitution, educational media, recreational facilities, religious appeals, competitions, and the training and development of Negro noncommissioned venereal disease control officers responsible for venereal

disease control in their units. These local programs have demonstrated the value of employing specially trained Negro personnel, both medical and lay, and the need for a direct and personalized approach.

CONCLUSIONS

In conclusion, the postwar period will present far greater assets for the control of the venereal diseases than have been available at any previous time, some of which are:

1. A tremendous number of physicians and lay personnel trained and experienced by the Army in the principles of venereal disease control will be available.
2. The dilution of the postwar population by 9,000,000 soldiers will raise the general venereal disease educational level to a new high, and it seems certain that future venereal disease control programs will be accorded increased public support. In this connection, efforts to reimpose a blackout on the venereal diseases are doomed to failure.
3. The remarkable advances in treatment, climaxed by the introduction of penicillin, will add great impetus towards achieving the goal of universal case finding and case holding.
4. Mass wartime experiences will add considerably to the venereal disease control armamentarium.

These factors, added to the stabilization of community life and the return of opportunity to follow the natural instincts of monogamous relationships, all lead to the conclusion that we will be presented with an unprecedented opportunity to reduce the incidence of the venereal diseases to a manageable minimum.

The Chairman: The next address wll be given by Commander W. H. Schwartz of the U. S. Navy.

VENEREAL DISEASE CONTROL IN THE U. S. NAVY

A Current Appraisal, with a Comparative Look at History and the Future

WALTER H. SCHWARTZ, *Commander (MC)*,
United States Navy
In Charge, Section of Venereal Disease Control
Bureau of Medicine and Surgery, Navy Department

It has been more than 5 years since the world was plunged into the abyss of active war by supermad Hitler; it has been almost 3 years since the sons of the once-Rising Sun ignited the wrath of America. These are longer periods of mobilization and active warfare than have ever before been experienced by the United States. The social consequences have been reflected in every facet of our culture—not least in the amount of venereal disease we have been able to assimilate and transmit.

Those who are familiar with the Navy's venereal disease record of World War I will appreciate the fact that it was then, for the first time in the history of wars, that the venereal disease rate fell. This was also the first war during which a concerted and reasonably scientific attack had been launched against the spirochete

and gonococcus. You will also appreciate, however, that immediately after the guns ceased firing in 1918 the rate shot up, within 1 year by 60 percent, although the actual figure was about one-third below the prewar level.

There are implications here for us today and for the future. If we match the last war's experience with this war's in terms of the over-all venereal disease rate for the entire Navy, or if we compare the rate level now with that of 1914, we might conclude that all goes well. The rate has fallen off sharply and now stands at the lowest point in Navy history, roughly 25 new admissions per 1,000 men per year.

Beneath that tobogganing curve, however, are concealed a complexity of development and circumstances. For example, this crude, all-Navy rate is a composite embracing rates for the total forces afloat and total forces ashore, the latter including the continental United States. Thus the general downward direction of the entire Navy rate reflects the very low rates now being experienced among substantial elements of our forces overseas. This is a condition which normally accompanies intense combat activity. However, as we consolidate our gains and as we go more deeply into the Asiatic

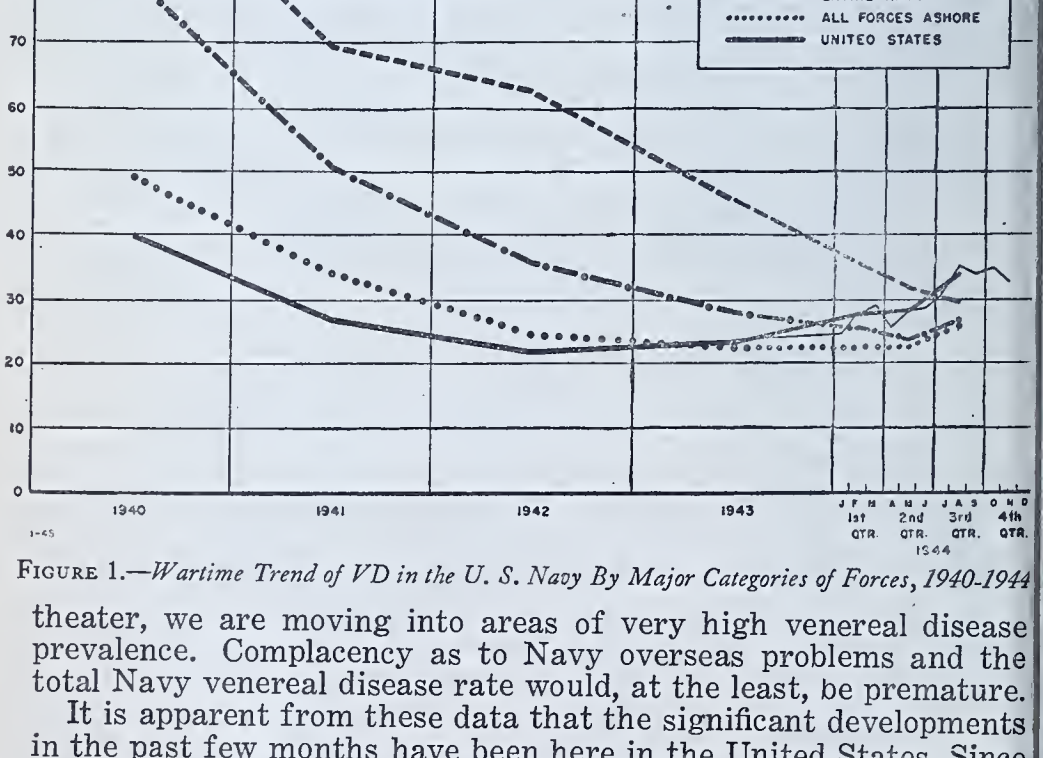


FIGURE 1.—*Wartime Trend of VD in the U. S. Navy By Major Categories of Forces, 1940-1944*

theater, we are moving into areas of very high venereal disease prevalence. Complacency as to Navy overseas problems and the total Navy venereal disease rate would, at the least, be premature.

It is apparent from these data that the significant developments in the past few months have been here in the United States. Since 1942, which it now appears was the low water mark, the admission rate has been climbing steadily and at an increasing speed. The 1943 figure of 24.5 per 1,000 was 9 percent above 1942. The record for the first 6 months of 1944 stands 11 percent above 1943, and

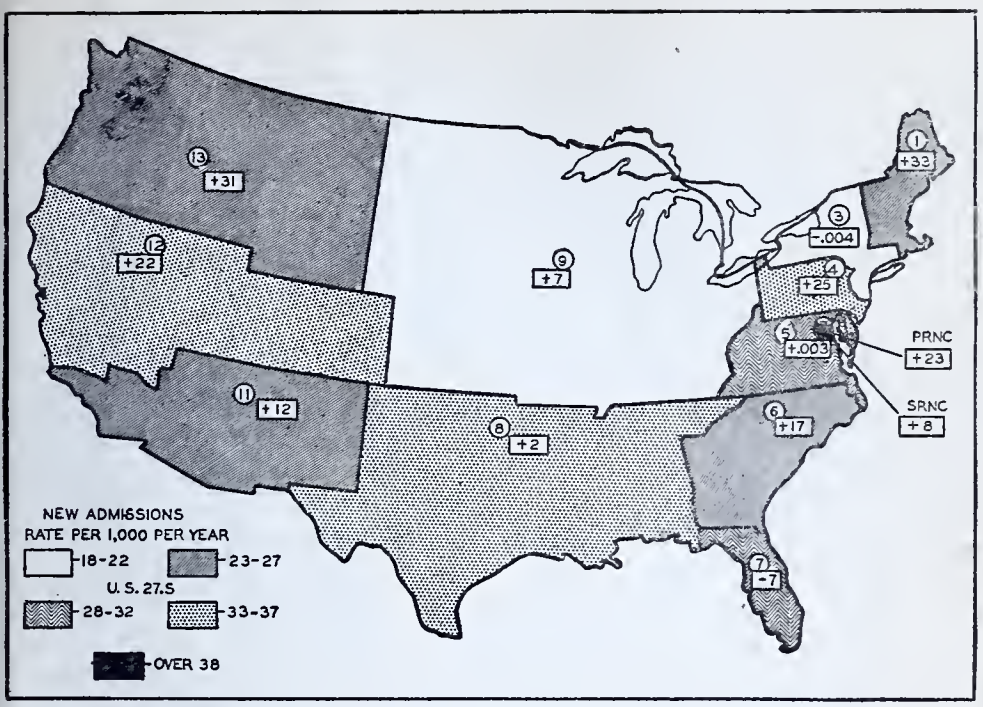


FIGURE 2.—*VD in the Navy—Continental U. S. January-June, 1944*
Admission Rates and Percent Change, 1943–1944

the rate—28—is above that of 1941. There is no lessening of the rate of increase, as may be seen in the tentative August figure of 36 for the Navy in the United States.[2]

The higher United States rates prevail along the east and gulf coast areas. In terms of the rapidity of increase, however, the west coast leads with a rise over 1943 averaging 22 percent. Surprisingly enough, the northeastern coastal area is next with a 19 percent increase, despite a very slight drop in the New York area. While rates are higher in the southeastern region, the rise has been only 8 percent, and the 7th District has recorded a 7 percent decrease. The southern area, the 8th Naval District, has been holding the line with a 2 percent rise, and the central region (District 9) is pulling up at a 7 percent angle.

As we all appreciate, the new admission rates of the Navy and the Army reflect quite accurately, and possibly more rapidly, the trend of venereal disease in the total civilian population because of the elementary fact that the bulk of venereal disease in the armed forces has its origin among civilians. Being strictly a new admission rate, recorded under circumstances which assure a high degree of completeness, such rates are perhaps more meaningful than civilian admittances and are obviously more significant than prevalence data.

Thus it may prove that the upsurge in the Navy venereal disease rate foreshadows the course America will follow in these coming months and years. It is an old path, a path made familiar during the World War I era, but this time we are apparently not awaiting

[2] See figure 1. The author supplies this addendum as of Feb. 2, 1945: "Monthly new admission rates per year per 1,000 Navy men in the United States have climbed steadily: July 31.19, August 35.91, September 33.84, October 35.41, and November 33.19."

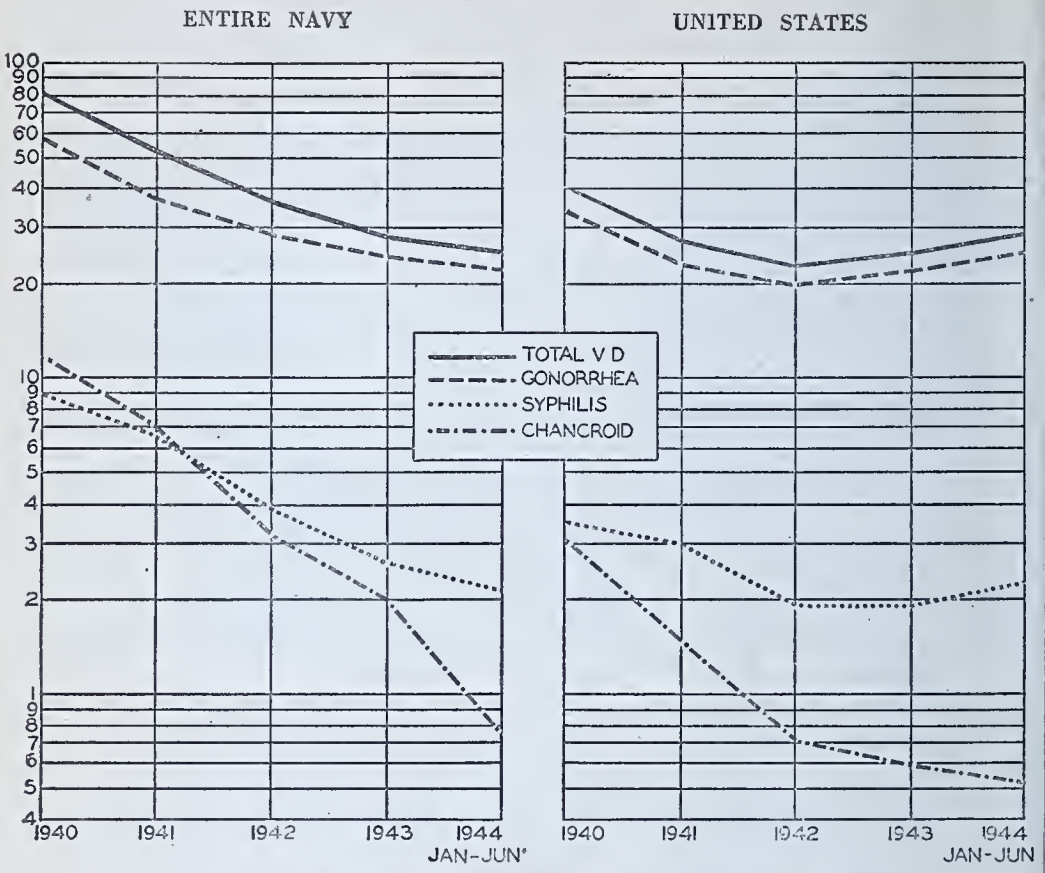


FIGURE 3.—*Wartime Trends in Gonorrhea, Syphilis, Chancroid and Total VD in the U. S. Navy*

demobilization to set out upon it. To be forewarned, however, is to be forearmed. There is no inevitable fate which dictates that we must continue along this path to ill health and social erosion.

Before a plan of action can be determined upon, it is necessary to identify the problem clearly. Additional light is thrown upon it when the Navy rate trends by disease are examined. Again, comparison between the Navy trend as a whole and the United States is without compliment to the States. All-Navy curves are continuing downward, although they appear to be leveling off somewhat. The reduction in chancroidal incidence from 11.7 in 1940 to 0.75 for the first 6 months of 1944 is encouraging, especially in light of the increasing number of personnel overseas.

Current levels in the United States, when compared to 1940, also appear quite favorable. Gonorrhea and syphilis new admissions for the January-June period of 1944 stood 25 and 36 percent, respectively, below 1940. Chancroid has decreased by 83 percent. Since 1942, however, gonorrhea and syphilis have increased in the United States by 21 and 16 percent, while chancroid has continued down by 25 percent. The total venereal disease admissions have risen 24 percent since 1942. Incomplete data for July and August of this year indicate that these upward trends are continuing.[3]

[3] The author supplies this addendum as of Feb. 2, 1945: "The continental trend continued upward during the second half of 1944. The tentative new admission rate for the 11 months ending Nov. 30, 1944 was 30.4 per 1,000 per year. This represents an increase of about 36 percent over 1942, and of 24 percent over 1943."

The influences behind these developments are most difficult of assessment. Undoubtedly, one of the most important is the changing character of the total social scene. Only inadequately can we either describe or appreciate it. The pressures pulling and hauling at our young people in and out of the armed services are well beyond our comprehension, at least in emotional terms. That they are powerful, there is no doubt. The lengthening of the war, the increasing disruption of normal home life, the heightening transiency of our population, the experiences which the men and women of the services are undergoing,—all these and others too enter into the picture.

The sum effect may be termed promiscuity. But that is an almost indecent and certainly inaccurate description of the problem. One of its more important manifestations is found among service personnel returning from combat duty overseas, pockets full of money, and impelled by months on end of grueling, dangerous life without the benefit of a woman's smile. Something of the same end result may be observed among the 'teen age girls, although these tendencies are by no means limited to any one age group.

But we cannot consider the cause and effect relationship here as due solely and merely to current psychologic disorientations. The bulk of Navy men are young—35 percent are under 20 and 67 percent under 25 years of age. The younger groups are still in the formative stages of their habits; most of the group under 25 are still close enough to home ties to reflect rather directly their upbringing. Manifestly the Navy can do relatively little in any direct sense to correct such deficiencies, although without question the total impression of Naval service upon the new sailor or marine is one of positive orientation toward a high ethical standard, a spirit of cooperativeness and self-respect. In the long run, the social habits of the sailor represent a projection of his home, school, and church training. The current venereal disease situation would suggest that the word "failure" is not contraindicated with respect to such training.

Newer and more efficient modes of treatment may be presumed to have a considerable influence upon exposure patterns. It may be that the few Navy men who in the past have tended to conceal infection may now be reporting for Navy treatment in order to obtain penicillin therapy. It may be that better treatment has tended to minimize the dangers of venereal disease in the minds of some. This latter assumption is subject to grave question, however, on at least two grounds: (1) That by and large the informational level of most patients appears to be rather low, and the likelihood of appreciating the significance of new therapy thereby is relatively low, and (2) that to assume promiscuity is significantly affected by fear of disease is to fly in the face of psychologic truths and general experience, and is to underestimate the overwhelming importance of other factors in the exposure syndrome.

The influence of Negro venereal disease rates upon the total continental rate is subject to some differences of interpretation. Negro rates are substantially higher than white rates. As one

Navy venereal disease officer put it: "Rates are higher in men who lack a sense of security as to their place in life, in their unit, and in the Navy." In one Naval District the Negro complement, amounting to 2.8 percent of the total, accounted for about one quarter of all admissions. There can be little question that data such as these mirror the venereal disease treatment and case-finding situation among our Negro citizens and reflect as well upon general social and recreational provisions for Negro servicemen. "The American Dilemma" does not fail to leave its mark upon venereal disease control.

Among Navy venereal disease control officers the general impression exists that civilian venereal disease control and social protective activities have relaxed somewhat in intensity in the recent past. The general complacency which now plagues the war effort in these crucial phases of combat likewise leaves its impression on venereal disease control. In some areas there are already reports of increasing prostitution activity, although the pattern remains predominantly "amateur."

Recent attacks upon the basic concepts of venereal disease control education have not contributed to a better public understanding of the problem and the urgency of its solution.

Possible countermeasures appear to fall under three headings: control programs within the armed services, control programs within the civilian community and, linking the two, contact investigation.

There is little need to elaborate here upon the Navy control program except in very general terms. With respect to treatment, preliminary field experience has demonstrated the wisdom of authorizing general use of penicillin in the treatment of all gonorrhea and of early and latent syphilis, insofar as supplies of that drug are adequate locally to meet other, more urgent demands. Under controlled conditions a pilot field trial providing new information as to the efficiency of chemoprophylaxis has been undertaken. Among some 25,000 exposures a gonorrhea failure rate of ¼ of 1 percent has been recorded. Education aiming at reduction of exposures and wider utilization of prophylaxis has been carried on since early 1944 along relatively new lines and directed primarily at the younger members of the Service who bulk so large in venereal disease reports. A more closely coordinated Army-Navy-civilian attack on venereal disease, prostitution and related problems has been facilitated by the recent establishment of Joint Army-Navy Disciplinary Control Boards in each Naval District and Army Service Command.

Insofar as civilian control efforts are concerned, it is hardly the place of a Navy venereal disease control officer to turn to blueprinting. As seen from this angle, however, it is certain that the low level of venereal disease rates in general has been the result of aggressive public health control and social protective activities. More of this is needed today. The rapid treatment center development has proved a signal step forward, and would seem to loom ever more important in the treatment era ahead.

The prime task of all, both as a wartime measure and in future terms, is clearly that of case finding. We have now the weapons, the know-how, and a considerable degree of energy with which,

it is not too much to say, we could eradicate venereal disease as a major public health problem in a matter of years, if not of months. The key is case finding, the cutting into the reservoir of infection.

Case finding largely devolves into two elements, one relying upon the individual voluntarily coming to examination and treatment, the other upon locating possibly infected persons through contact operations. Voluntary reporting is basically a matter of public education, an honest education which brings to every individual the essential facts about venereal disease and its broad implications, with emphasis on the fact that it is a disease for which there is a cure. The time of eradication of venereal disease may very well be set by the degree to which we carry out this educational function, and the extent to which treatment facilities are available for rapid and efficient treatment.

Contact investigation, as the second basic element in case finding, has come into sharp focus in recent years by virtue of its inherent potentialities and by the development of large-scale contact referral systems by the Navy and Army. We have all approached this operation in a highly empirical manner, and with a concentration of attention upon those elements most significant to our practical needs. In the developing phase in which we now find ourselves, however, it would seem particularly desirable that some fundamentals be clarified, some assessment of responsibilities made, some energies expended to improving the procedures and actual operations.

Underlying any real progress in this field, however, is the necessity for some unity as to concepts and terminology. It is most difficult to discuss and solve common problems when the persons in the discussion are talking about similar though different things in different languages. It may be useful to dissect this contact operation to find out what it comprises and to provide some common ground for consideration.

One practicable analysis considers the contact operation under the term contact investigation. This embraces four progressive steps: (1) The contact-education interview where the patient is reorientated and reeducated with the objective both of inhibiting repeat infections and of obtaining pertinent contact information; (2) contact reporting, where the report form is forwarded to the appropriate agency for action; (3) contact location, where the alleged contact is searched for, and finally, (4) contact disposition, where the contact is examined and, if found infected, becomes a new patient and the process begins anew with a contact-education interview.

This nomenclature has proved useful in the development of a training program for Navy personnel handling contact reports and conducting contact-education interviews. Clarification of the broad concepts and terminology would do much to shift attention to the more immediately important operational areas.

One of the more important, from the point of view of the Navy, is that of contact-education interviewing. This and contact reporting are the primary responsibilities of the armed services in contact investigation. Conversely, contact location and disposition are the pressing problems for civilian agencies insofar as military contacts are concerned. Toward the improvement of interviewing,

the Navy is now engaged in development of a training plan which endeavors to transmit to large numbers of medical department personnel the basics of interviewing. Similar attention might well be given to field handling of contact reports by civilian health agencies.

This latter comment is prompted by Navy experience during the past 4 months with the new uniform system of venereal disease contact reporting. Conclusions can be only very tentative, but in general the acceptance of the system on the part of civilian and Navy medical personnel has been gratifying and successful. In but a few instances have indications reached us of failure to understand or to carry through obligations on the part of civilian agencies.

A random sampling of 1,000 of these new contact reports has been made which throws some light on the nature of our problem. The sample is reasonably representative, although it was taken from reports completed during the early days of the new system and is probably, therefore, somewhat below present levels of operation, both naval and civilian. The expected pattern—youth, pick-ups, home or hotel exposures, no prophylaxis—is found.

Of importance here, however, is the fact that an attempt is being made to evaluate such reports on an objective basis as to completeness of information and, indirectly at least, as to the efficiency of interviewing. One of the most meaningful evaluations is with respect to the degree of completeness of the contact's name, address, and place of employment.

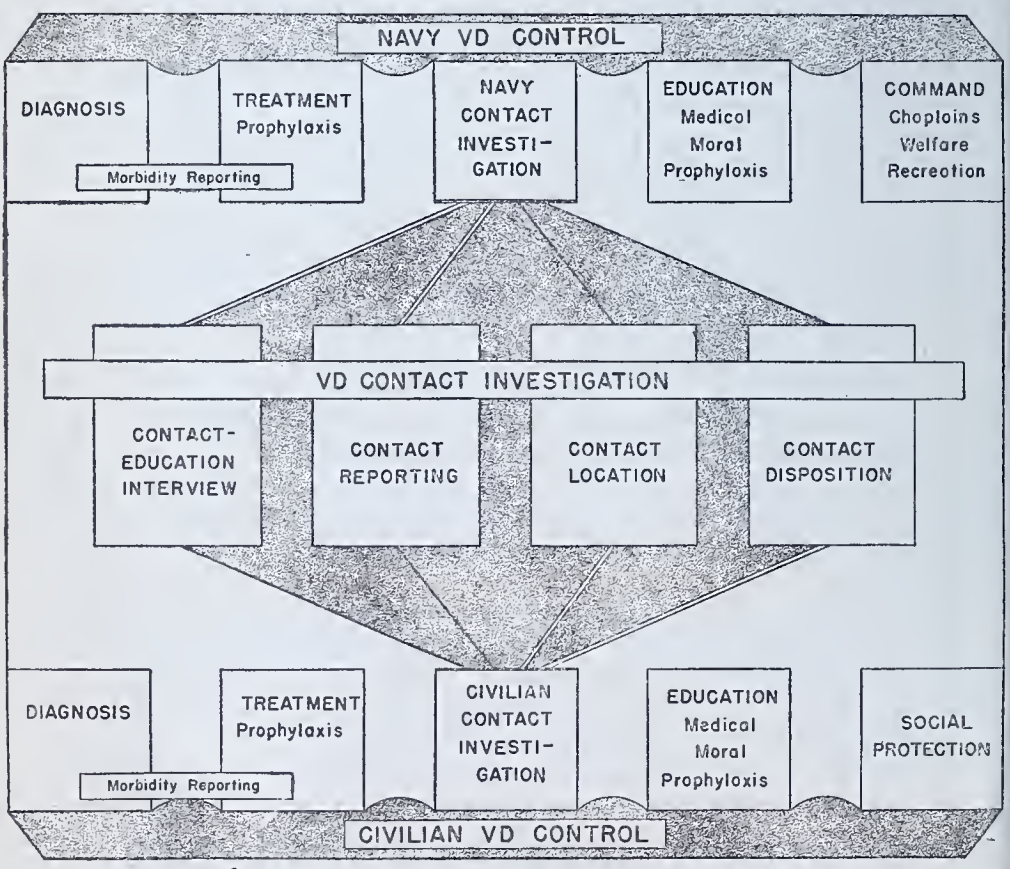


FIGURE 4.—*VD Contact Investigation—Its Place in VD Control*

Identification data were considered excellent if these elements were given completely, or approximately so. Such was the case in 7.5 percent. Less complete but still quite adequate information was reported in 19 percent. The remaining 73 percent were considered only fair, with more than half of the total probably worthless so far as this particular item was concerned. Admittedly, these figures are not favorable, and we intend to improve them materially.

From the civilian health department standpoint, results of contact location and disposition were as follows: 22 percent of the reports had not been returned within the 8 weeks allowed for follow-up; 50 percent were considered insufficient to start investigation, and 7 percent more proved to be insufficient after a location attempt; 14.2 percent were found; 9.2 percent of the contacts were infected; 6.9 percent were new cases brought under treatment as a result of this contact investigation; 4.6 percent were found to be not infected. In other words, of the 142 cases found, 48 percent were brought under treatment as a result of the investigation.

The Navy estimate of adequacy compared with the health department's estimate appears to correspond reasonably well. Practically all of those contacts found were evaluated quite high. However, the bulk of those reports not yet returned by health departments were evaluated very low and there would seem little cause to hold them out.

Even these very preliminary data serve again to underscore the interdependent nature of venereal disease contact investigation and, indeed, the whole of venereal disease control. No program is stronger than its weakest element.

This conference is rightly concerned with the future of venereal disease control and with the problems the postwar era will present. We are indeed fortunate that we have a new therapeutic armamentarium which holds so much promise. It likewise offers challenges. One challenge points to what appears to be the almost inevitable necessity for large-scale expansion of treatment facilities which are known by and available to every individual in this Nation who might have need of them. The future of venereal disease control clearly lies in treatment for all.

A second challenge is swallowed up in what may prove to be a coming wave of moral reaction, already foreshadowed. Experience should have taught us that morals and ethics cannot be enforced by authoritarian methods. The answer more nearly lies in a broad understanding and compassion for human frailties which in the process of application respects the democratic dignity and self-respect of all persons, benighted as some may perhaps appear.

The trend of venereal disease in the United States today gives warning of the approaching storm. Venereal disease can be no matter of national disinterest when the facts are known that since World War II began the Navy has suffered 200,000 preventable venereal disease casualties at a loss of two million man-days. We cannot afford to relax our control efforts nor to fall back to a laissez faire approach to the broad problems. We cannot permit the United States to regress in this or any other field while it remains, as it must, in the spotlight of civilized progress.

The venereal disease control program must be intensified and expanded in the medical facilities field, in public and professional

education, and basically, in the field of contact investigation. There is no more direct means of finding new cases than in identifying and bringing to treatment the contacts of known cases. It is not too much to set our sights on the goal of "every physician a contact-education interviewer."

Venereal disease is an international problem. In the days to come we shall all appreciate more vividly the significance of high venereal disease prevalence in Singapore, Naples, Berlin, and Tokyo. Today we in the Navy face problems of exactly the international character that all of us will meet in the future. Today we in the Navy must lay our plans in terms of an extended period of active Pacific warfare. We can only be apprehensive that the partial demobilization which presumably will follow "Victory in Europe Day" may prove a partial demobilization of venereal disease control. "V-E" Day must not become "V-D" Day.

The opinions or assertions contained herein are the private ones of the author and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

THURSDAY AFTERNOON SESSION

November 9, 1944

The meeting reconvened at 2:15 o'clock. Dr. Thomas Parran presided.

The Chairman: This afternoon we are to have a symposium of three presentations on penicillin. The first paper will be given by Dr. Joseph Earle Moore, of Johns Hopkins University.

PENICILLIN IN EARLY SYPHILIS[1]

JOSEPH EARLE MOORE, M. D., *Associate Professor of Medicine,*
Johns Hopkins University
Chairman, Subcommittee on Venereal Diseases,
National Research Council

After the demonstration in June 1943, by Mahoney and his associates that penicillin is active in syphilis, the need of the armed forces brought about a cooperative study of the drug in both early and late syphilis under the auspices of the Committee on Medical Research of the Office of Scientific Research and Development, beginning in September 1943. The Army, the Navy, the Public Health Service, and about 20 selected civilian clinics have participated. These groups have agreed to examine and treat cases by designated systems, to record results on appropriate forms, and to transmit forms to a statistical center.

Data regarding about 4,000 of 4,479 patients so far treated for early syphilis are available for statistical study as of Nov. 1, 1944. Only 406 patients have been followed up for as long as 6 months, only 1 for as long as a year.

From the beginning of the study, with variation in dosage between fortyfold range of 60,000 to 2,400,000 units, it was obvious that in early syphilis the immediate effects were identical regardless of dose, in terms of disappearance of surface organisms, healing of lesions, and trend toward reversal of blood serologic test. Disappearance time of Treponema pallidum, healing of lesions, or serologic reversal, therefore, could not be used as criteria of successful therapy. The only remaining useful criterion was relapse, infectious mucocutaneous relapse, or serologic relapse, which does not tend to occur in important numbers until about the fourth month after completion of treatment. The incidence of clinical or serologic relapse is in inverse proportion to the total dose of penicillin administered every 3 hours day and night over a period of 7½ days. Highest relapse rate is with minimum dose employed, 60,000 units, where nearly 60 percent of patients already have relapsed. Relapse rate for 300,000 unit dose is about 36 percent, for 600,000 units, 23 percent, and for 1,200,000 units, at the end of about 7 to 8 months, 7.1 percent. The relapse rate for 1,200,000 units varies with the stage of the disease; it is about 2 percent in patients with seronegative primary syphilis, about 4 percent with seropositive primary syphilis, and about 15 percent in those with secondary syphilis.

[1] The material published herewith is an abstract of the stenographic report of Dr. Moore's paper. Publication of the full report has been withheld at the author's request because of the tentative and incomplete nature of the clinical and statistical data at the time it was presented.

Two small series of patients were treated over a 7½-day period with 60,000 and 300,000 units of penicillin, respectively, plus a known subcurative dose of mapharsen, 320 milligrams given in single injections of 40 milligrams each day. The group with 60,000 units of penicillin plus mapharsen have a significantly lower relapse rate than do groups given 60,000 units of penicillin alone; the group given 300,000 units of penicillin plus mapharsen experienced a relapse rate comparable to that from 1,200,000 units of penicillin alone.

Data are presented regarding the percentage of patients treated by different schemes who have become seronegative within different periods of time up to about 8 months. Of the patients receiving 60,000 units of penicillin alone, 42 percent have become seronegative within 8 months. About 56 percent of each of the groups receiving 300,000, 600,000 and 1,200,000 units of penicillin and 60,000 units of penicillin plus mapharsen, became seronegative within about 8 months. The highest proportion of persons becoming seronegative was in the small group given 300,000 units of penicillin plus mapharsen. All these results are preliminary, and based on short observations of a small number of patients; therefore, it is assumed that relapse rates eventually will be considerably higher in each group.

The optimum method of use of penicillin in early syphilis has not been determined. Several variables remain to be explored, including the effect of much larger doses, which have been employed in the Army and the Navy, where a total of 2.4 million units of penicillin is administered in a course of injections, one every 3 hours day and night, over a period of 7½ days. It has not been established as yet whether this arbitrarily selected large dosage is more or less effective than smaller dosages. Also needing exploration is the effect of prolonging the interval of treatment beyond 7½ days, the combination of penicillin with other agents such as mapharsen, bismuth, and fever, and methods to prolong the absorption and excretion of penicillin to reduce frequency of injections toward an ambulatory treatment basis.

This organized study of penicillin in syphilis presents an opportunity to accomplish at relatively small cost, within perhaps 5 years, something which has not heretofore been accomplished in the treatment of syphilis during 450 years of its existence—to determine the optimum method of treatment of early syphilis with the great advantage of possible eventual eradication of the disease.

The Chairman: My attention has just been called to the fact that we have on the program this afternoon three of the original members of the Cooperative Clinical Group. This group, you may recall, consisted of Dr. Moore, Dr. Stokes, Dr. O'Leary, Dr. Wile, and Dr. Cole; four of these five members are present at this conference, Dr. Cole being absent.

The next paper on the program will be given by Dr. John H. Stokes, of the University of Pennsylvania.

PENICILLIN IN LATE SYPHILIS[2]

An Interim Report

JOHN H. STOKES, M.D., *Professor of Dermatology & Syphilology,*
with the collaboration of
HERMAN BEERMAN, M.D.,
NORMAN R. INGRAHAM, JR., M.D.,
JOHN W. LENTZ, M.D.,
HENRY G. MORGAN, *Surgeon* (R) USPHS,
GEORGE D. GAMMON, M.D.,
WILLARD STEELE, M.D.,
ELIZABETH KIRK ROSE, M.D.,
PAUL GYORGY, M.D.
University of Pennsylvania

The assignment of a topic of this sort recently reviewed elsewhere would be largely repetition were it not for some attempt at originality in the presentation of the material. An incorrigible fondness for the parallel column has led me to put the substance of the University of Pennsylvania group's experience into this particular form.

The purpose is, then, to supplement terse and somewhat dogmatic statements with case material which after all, is what carries the touch of conviction in late syphilis far more than in early syphilis. The individualization which treatment of late syphilis requires, makes attempts at statistical evaluation, especially at this stage of small case numbers and relatively short periods of observation, much less satisfactory.

If you will turn now to figure 1, the parallel column, discussion of *what we know* and *what we want to know* will begin.

Figure 1.—PENICILLIN ALONE IN LATE SYPHILIS

What we know	What we want to know
1. Penicillin in low dosage (300,000-600,000 O.u.) cures soft tissue gumma, simple uncomplicated bone lesions in absence of sequestrum formation. No effect on Charcot joint.	1. Does low or inadequate dosage based on skin or bone lesions activate a more serious concomitant complication (i.e. neurosyphilis)?
2. Herxheimer or therapeutic shock occurs in late syphilis and may be serious; should be avoided.	2. Does therapeutic paradox occur—i.e. in hepatic or cardiovascular syphilis?
3. There is little evidence in late syphilis that "inadequate" dosage puts the patient in a "sensitized" position (Unstimmung) with respect to relapse and progression.	3. Can we use repeated courses with safety; (a) at lower total dosage levels provided (b) the individual injection dose produces a high enough level in the central nervous system?

[2] The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Pennsylvania. All material of this report is based on contributions from the Hospital of the University of Pennsylvania, the Philadelphia General Hospital, the Pennsylvania Hospital, the Children's Hospital of Philadelphia, and the individual special departments constituting a penicillin panel.

4. Penicillin alone may favorably affect any type of active neurosyphilis, symptomatic and unsymptomatic;

4. Are the failures due to time-dosage relationships, inaccessibility of the process (island lesions), inadequate duration of treatment, need for localizing (intrathecal) or supplementary nonspecific (fever) methods, or host or penicillin inadequacy?

5. In dosage as low as 1,200,000 O. u.;

5. See tabular comparison of 1,200,000 and 2,400,000 to 4,000,000 O.u. dosage scales.

6. With prolongation of effect up to 235 days;

6. Will one mild push plus his own defense and reaction push the patient permanently over the hump?

7. Even to Grade 3 and 4 improvement of symptomatic simple demented paresis, and of Type III spinal fluids with preparetic formulas;

7. What part does spontaneous remission play?

8. In spite of the previous failure of vigorous routine As-Bi and intraspinal therapy.

8. Greater penetration or tissue diffusion of penicillin, greater spirillicidal efficiency per milligram, a combination of spirillicidal and nonspecific effect?

9. Penicillin produces better immediate results than the arsenicals, at less risk, and in much shorter time.

9. Will results last as well as in the As-Bi, tryparsamide, fever and fever-As combinations?

10. It does the same in comparison with the pentavalent arsenicals.

10. Should it be used in postfever therapy and as a final fillip to patients who have had an extended routine (for good measure)?

11. It should replace them both.

11. Is it too soon to say that?

12. The value of high single course treatment total dosage (2,400,000 to 4,000,000 O.u.) as compared with lower dose repeated courses (1,200,000 O.u.) is not yet determined, but the lower dosage scales can be tried without hesitation, if observation is maintained.

12. Is the crux of the matter in the 20,000-40,000 individual (meningeal penetration?) dose, or will prolongation of treatment be the clue ("Prolongation is as important as mass")?

13. Penicillin's status with reference to fever therapy is undetermined but in process of study.

13. How long and how controlled must be the study of this question?

14. Penicillin has "tonic" properties (postpenicillin weight-gain, well-being, etc.).

14. How expressive is this of possible important byeffects on focal and intercurrent infection, etc.?

15. It influences refractory and little understood symptoms like lightning pains at least as much as other current methods and at times succeeds when these have failed.

15. Where is the point and what the mode of action in pains and crises? On the spirochete, on focal infection, by suggestion, etc.?

16. It has thus far, less than 50-50 efficiency in interstitial keratitis, and the therapeutic effect is erratic and unpredictable.

16. Is interstitial keratitis an infection-allergic process which penicillin may affect unfavorably (induction or accentuation)? Is it a matter of dosage, duration, antecedent complication and damage?

17. It may arrest progression in primary optic atrophy with short observation; has thus far blinded no one; may produce slight improvement in vision and fields; may return the spinal fluid to normal, including Type III; may fail (in lower dosage) to stop a localized chiasm lesion, despite such spinal fluid improvement.

17. How big are the factors of time, subjectivity, possible local inflammatory precursors and concomitants (chiasm meningitis, retrobulbar neuritis)?

18. In serologic fastness at moderate dosage, penicillin is erratic and not notably effectual (few cases).

18. What is serofastness? Penicillin may help prove it scar or active process.

19. Penicillin seems perhaps more promptly and markedly effective against the abnormal spinal fluid than the seropositive blood.

19. Like a pentavalent arsenical?

20. Impending relapse can be recognized in spinal fluid by rises in cells, protein, Wassermann and colloidal curves, and Dattner-Thomas normals are sometimes reduced to absolute normals.

20. What is a normal cerebrospinal fluid after any form of treatment? Can penicillin improve on Dattner-Thomas normals, thus indicating them abnormals?

21. It is possible with penicillin to reduplicate traditional experience with nonconcomitance of serologic and clinical findings and progress and as regards blood and spinal fluid findings.

21. Is there an insignificant and irreversibly abnormal spinal fluid over the years, without progression of the process?

22. It is not possible to rehabilitate wrecks or advanced deteriorates, or to replace dead or scarred tissue by normal, with penicillin.

22. How define the clinical and serologic deadline? Are the deaths and unfavorable courses unfavorably influenced or hurried by penicillin?

23. Penicillin reactions while minor, are not negligible in late syphilis. The Herxheimer reaction in a focal lesion in a vital structure may be grave. Initial halving of the first and even second day dosage is advisable. The reduction should be compensated by prolongation of course.

23. Does dosage reduction really influence reaction, and if so, how much; and does temporary reduction impair ultimate effect?

24. Urticaria and severe transient gastro-intestinal reaction and exfoliative dermatitis in previously treatment-intolerant patients have been observed. Some degree of sensitization in occasional individuals should be watched for.

24. What will be the significance for treatment of induced allergy to penicillin? What the role of impurities, mixtures of strains, variations in molecular constitution, the patient's allergic status, and background?

25. The question of lot variation, potency variation and variability of penicillins as such obtained from various strains and by various processes should be closely studied, especially if therapeutic results are unsatisfactory in a promising case. If possible, a course of penicillin should all be from the same lot.

25. The answers are in the air!

26. An effort must be made to disentangle specific and nonspecific effects of penicillin and to identify intermediate body mechanisms involved in penicillin action and failures.
27. No preparatory treatment other than modification of penicillin dosage scale is called for in the types of late syphilis discussed.

26. How do they compare with those of the arsenicals and bismuth? A measure for therapeutic tests?
27. Will experience with hepatic and cardiovascular syphilis prove the old preparatory methods still useful (penicillin being too much like an arsphenamine)?

FIGURE 2.—*Response of possible nonsyphilitic lesion to penicillin in a latent syphilitic. Note serologic response*

Acute gangrenous balanitis in latent late syphilis

CASE #1, J. R., W., M., age 43. Darkfield positive seropositive primary syphilis in 1933; total treatment administered regularly was 114 arsenical and bismuth. Persistent positive blood serologic tests prepenicillin; negative CSF; Frei and chancroidal tests negative at start and 3 months later; repeated darkfields negative; repeated gonococcal smears negative. Mixed strep-staph by spread and culture and fusiform bacilli but no spirochetes. Blood count and blood sugar values within normal limits; locally saline dressings only.

Amount of penicillin administered 392,500 O. u., at 12,500 units every 4 hours.

Date	Days post-pen.	Kolmer Wass.	Quant. Kline diag. units	Eagle flocc.
11–11–43	0	444000	16	positive
11–16–43	5	444000	32	positive
12–1–43	20	443000	64	positive
12–17–43	36	441000	4	positive
1–5–44	55	110000	0.25	negative
2–4–44	85	410000	0.5	doubtful
3–3–44	113	000000	neg.	negative
5–10–44	181	000000	neg.	negative
7–29–44	261	000000	neg.	negative
10–24–44	348	000000	neg.	negative

IGURE 3.—*Contrast between response of soft tissue gumma and osteomyelitic bone in nasopala tine structures*

Gumma, nasopalatine, soft tissue, vs. osteomyelitis of nasal bones and skull in syphilis

ASE #10, H. M., W., F., age 69. Gummatous ulceration and perforation of soft palate. Increased density, bony palate.

PENICILLIN 1,200,000 O. u. in 8 days

Days post-penicillin	Blood Kline units	Notes
0	32	
11	64	Biopsy, not malignant.
18		Spinal fluid negative.
26	128	
34		Edges healing, perforation smaller.
46	64	
49		Perforation healed, open.
60	64	
83	64	
109	64	
130	64	
144	64	Prosthesis with obturator inserted.
170	64	
205	64	Normal speech with obturator. Complete healing.
284	128	
313	64	

CASE #122, R. S., M., W., age 30. Gummatous osteomyelitis, sinuses and frontal bone, previous As-Bi treatment, no effect.

PENICILLIN 2,400,000 O. u. in 10 days

Days post-penicillin	Blood Kline units	Notes
0	128	Herxheimer 100.4°F.
25	128	Spinal fluid negative
101	64	No improvement.

FIGURE 4.—*Same strain of organism in two individuals, a brother and sister with congenital syphilis, under penicillin*

Congenital syphilis in brother and sister under penicillin

CASE #5, Brother, R. B., W. age 24. Asymptomatic neurosyphilis Grade III CSF; typical stigmas; accentuated deep reflexes.

PENICILLIN 1,200,000 O. u.

Days post-pen.	Blood Kline units	Spinal fluid findings			
		Cells	Prot.	Wass.	Mastic
0	128	22	4+	1244	1333200000
9	128				
19	16	8	3+	1244	4431100000
40	32	55			
55	64	4	±	0012	2221000000
86	64	3	30mg.	0123	2221100000
111	64	1	15mg.	0124	2211000000

PENICILLIN 1,200,000 O. u. Retreatment 123 days postpenicillin

135	64	2	40	0011	2211000000
164	64	4	20	0011	1110000000
227	64	4	30	0011	1111100000
325	128	2	40	0112	2221100000

Impending relapse? Penicillin resistance or "Unstimmung" developing?

CASE #109, Sister, L. B., W., age 15. Interstitial keratitis; C. N. S. negative; spinal fluid normal. Typical dental stigmas.

PENICILLIN 4,000,000 O. u.

Days post-pen.	Blood Kline units	Notes
0	64	Severe bilateral I. K. unaffected by 4 maph-arsen, 4 Bi. Improved during penicillin course. Clearing began OS in 7 weeks; OD in 9 weeks post-penicillin. In 13 weeks, OD 6–20, OS 6–12. No activity, peripheral clearing, small central opacities.
28	128	
43	128	
55	32	
68	64	
101	64	

Although the 2 eyes were involved within 2 days of each other, the second eye to become involved made much the better progress

FIGURE 5.—*Serologic success and failure in serofastness, congenital syphilis under penicillin*

Congenital syphilis—Wassermann-fast

CASE #24, A. H., M., C., age 12. Clinically negative; negative spinal fluid, retained positive serology. Total prepenicillin treatment: Stovarsol 280 gm.; Sobisminol 95.2 gm ; 197 gm. sulph-arsphenamine; 2 intravenous arsenicals and 8 intramuscular bismuth subsalicylate.

Days post-penicillin	Blood Kline units
PENICILLIN 600,000 O. u.	
0	32
17	32
32	32
52	8
65	16
79	32
107	16
135	32
178	32
PENICILLIN 1,200,000 O. u. (retreat.)	
186	[1]0.25
198	0.25
250	0.25

CASE #31, L. S., F., W., age 34. Stigmata and atrophic arthritis. Total prepenicillin treatment: 31 arsenical, 343 bismuth subsalicylate, 95 tryparsamide; negative spinal fluid, recurrent interstitial keratitis but otherwise clinically negative. No treatment for 2 years prepenicillin; retained positive serology.

Days post-penicillin	Blood Kline units
PENICILLIN 1,200,000 O. u.	
0	64
13	32
20	32
36	64
89	8
120	32
168	32
PENICILLIN 2,000,000 O. u. (retreat.)	
200	32
Results from second course not yet available	

[1] Practically negative

FIGURE 6.—*Equivocal results in blood serologic reactions under penicillin in congenital syphilis*

Blood serology in late congenital syphilis

These cases are predominantly retreatment cases—1,200,000 O. u. to 5,200,000 O. u. Observed over a period of 64 to 325 days.

18 CASES:

Improved	1
Improved and relapsed, fairly high titers	5
Fluctuating	4
Reversed to negative	3
Reversed to plus-minus	1
Herxheimer (not reversed)	1
No change (negative at start)	2
Worse	1

Total of only 5 improved, 163—282 days.

Evaluated:
October 1944

FIGURE 7.—*Erratic, 50-50 response of interstitial keratitis to penicillin*

Interstitial keratitis, late congenital syphilis

7 CASES

Observation	Previous treatment	Penicillin dosage	Results postpenicillin
97 to 316 days	1 none	1,200,000 1	
1 case 316 days	1 little	1,700,000 1	No change 4
5 cases 195–286	1 much	2,400,000 2	
2 cases 97–103	4 with fever	4,000,000 2	Improved [1] 3
		5,200,000 1	

[1] #6, L. S., 1,200,000 O. u.; #72, R. B., 2 x 1,200,000 O. u.; #109, L. B., 4,000,000 O. u.

Evaluation:
October 1944

FIGURE 8.—*Penicillin response of serofastness in late latent syphilis is not encouraging thus far*

Serofastness in late latent syphilis (not including congenital syphilis)

10 CASES:

Penicillin Dosage	
1,200,000 O. u.	8
2,400,000 O. u.	1
400,000 O. u. only, with reversal to negative	1

Results	
Improved	2
Improved with relapse	1
Cleared	1
Fluctuating (2 with initial Herxheimer rise)—including 1 case that had had 2 5-day drip courses	6

Prepenicillin data on 8 of 10 cases above

1	2 5-day drip; no improvement.
2	scattered small amounts of treatment with up-down improvement.
3	40 As., 40 Bi.
2	untreated, unchanged, up-down.

At 1,200,000 to 2,400,000 results in serofastness are not encouraging—erratic, fluctuant, no relation to previous treatment

Evaluated:
October 1944

FIGURE 9.—*Note the superiority of over-all spinal fluid as compared with clinical results. These figures unless broken down by types of neurosyphilis are suggestive only*

Over-all results, neurosyphilis, all types, by dosage scale

PENICILLIN 1,200,000 O. u. in the first course

Status of patient after that course and before any retreatment

SYMPTOMATIC RESULTS

Cases	Improved	No change	Improved and relapsed	Worse
34	12 One-third minus	15 One-half	3	4

CEREBROSPINAL FLUID RESULTS

46	33 Two-thirds plus	10 One-fifth	2	1

PENICILLIN 2,400,000–4,000,000 O. u. in the first course

Status of patient after that course and before any retreatment

SYMPTOMATIC RESULTS

29	17 One-half plus	9	3	0

CEREBROSPINAL FLUID RESULTS

29	19 Two-thirds	8	1	1

The striking feature of this chart is that 1,200,000 O. u. does so much. Longer observation may of course show that 2,400,000 to 4,000,000 O. u. in one course ultimately does more or holds the result better. Perhaps on the other hand, adequate levels in the nervous system are reached by 20,000 O. u. x 8 hours x 7½ days for good results.

Evaluation:
October 1944

FIGURE 10.—*Five out of six grade II and six out of ten grade III spinal fluids in asymptomatic neurosyphilis showed improvement in cell count and protein, or better*

Grade I, II, III asymptomatic neurosyphilis

Spinal fluid	No. change	Relapse	Worse	Improvement (grade)			
				1	2	3	4
Grade I 0							
Grade II 6	1				2	2 1 DT	1
Grade III 10	3 1 DT. 1 R.		1		3 1R	2 1R	1 1R

Blood serologic responses

Herxheimer	7
To negative	1
Fluctuating	2
No change	4
Improved and relapsed	2

R – Retreatment
DT– Dattner-Thomas "inactive" fluids

Evaluation:
October 1944

FIGURE 11.—*A type III spinal fluid reduced to a complete normal by 2,400,000 units of penicillin. Note reduction of a Dattner-Thomas inactive to flat negative*

ASYMPTOMATIC NEUROSYPHILIS

CASE #8, L. S., W., F., age 41. Red Cross donor positive STS July 1943, no history of infection or previous treatment. Duration of follow-up 310 days.

PENICILLIN 1,200,000 Oxford units

Days post-penicillin	Blood Kline units	Spinal fluid findings			
		Cells	Protein	Wassermann	Mastic
0	64	103	4 +	4444	2444411000
17	8	29	2 +	1244	2221100000
46	32	11	1 +	0012	2211000000
74	32	6	30 mg.	0112	1111000000
102	32	6	40	0112	2211000000
129	8	4	30	0011	1111000000
159	32	8	30	0122	2211100000
178	16	6	30	0012	2221100000
PENICILLIN 2,400,000 Oxford units (retreatment)					
186	4	7	20	0000	1111000000
310	32	3	30	0000	1110000000

FIGURE 12.—*A type III spinal fluid in congenital asymptomatic neurosyphilis, reduced to flat negative with a second course of 1,200,000 O. u. after reduction to a Dattner-Thomas inactive fluid by a first course of 1,200,000 O. u.*

Congenital syphilis—Asymptomatic C. N. S.—Grade III spinal fluid

CASE #50, R. H., W., M., age 25. Typical stigmas. 1939: Routine BWR positive; 1939–1942: Treatment—62 As, 102 Bi.

PENICILLIN 1,200,000 Oxford units

Days post-penicillin	Blood Kline units	Spinal fluid findings			
		Cells	Protein	Wassermann	Mastic
0	16	96	40 mg.	4444	2455555000
8	neg.	21	20	4444	4444210000
36	32	12	30	0124	2221000000
PENICILLIN 1,200,000 Oxford units (retreatment)					
53	neg.	9	30	0112	2221100000
143	32	1	20	0000	1111000000

FIGURE 13.—*A Dattner-Thomas inactive fluid, unaffected by penicillin*

CASE #30, A. B., C., F., age 58. Positive STS 1935, lymphogranuloma venereum, rectal stricture. Grade 3 CSF. 1941—12 As, 86 Bi., 91 tryparsamide Hypertension, dull mentality, AR pupils, diminished deep reflexes. Resistant spinal fluid, no response to varied treatment, including penicillin. "Dattner-Thomas type normal".

PENICILLIN 1,200,000 Oxford units

Days post-penicillin	Kline units blood	Spinal fluid findings			
		Cells	Protein	Wassermann	Mastic
0	+1	6	3+	4444	2355331000
8	Neg.	4	2+	0124	1221000000
39	Neg.	2	30 mg.	4444	2335421100
67	Neg.	3	30	1122	2332210000
102	¼	5	30	0112	1221110000
137	¼	1	20	0112	2221100000
179	Neg.	3	30	1244	2444331100
PENICILLIN 2,400,000 Oxford units (retreatment)					
242	Neg	2	30	2344	3444220000
262	½	2	30	1244	3444210000

FIGURE 14.—*Response of a meningovascular neurosyphilis clinically and serologically to 1,200,000 O. u. of penicillin*

Neurosyphilis, 3d nerve, grade III spinal fluid

CASE #52, R. R., C., M., age 32. Diplopia 1944, headache, slight anisocoria, 3d nerve weakness.

PENICILLIN 1,200,000 Oxford units

Days post-penicillin	Blood Kline units	Spinal fluid findings			
		Cells	Protein	Wassermann	Mastic
0	128	30	40 mg.	4444	4555553110
33	64	5	20	2344	3321100000
82	32	10	20	0112	2211000000
124	8	5	20	0012	2211100000
166	4	3	20	0000	0000000000
235	neg.	3	10	0000	1100000000

235 days postpenicillin, normal eyes, no headache. Third nerve normal

FIGURE 15.—*Response of primary optic atrophy in tabes, under penicillin*

TABES DORSALIS WITH PRIMARY OPTIC ATROPHY

(Question of retrobulbar and chiasm meningitis)

13 CASES:

Observation		Clinical symptoms	
Over 300 days	1	Worse	2
Over 200 days	8	Unchanged	6
Over 100 days	2	Improved (may be temporary or slight)	3
Less than 100 days	2	Improved with relapse	1
		No data	1

Cerebrospinal fluid changes

	First course- 1,200,000	Second course- 1,200,000	Third course- 4,000,000
Improved but still abnormal cells and protein	3	1	
to Dattner-Thomas inactives	4		1
to negative fluid	3	3	
No change	0		
Worse	0		
Up-down	0		
Relapse after negative	0		
after Dattner-Thomas inactives	1		
Negative at start	1		
Herxheimer	0		
No data	2		

Summary

Of 13 Cases, 10 Showed CSF improvement with the first course.
4 Became Dattner-Thomas normals.
3 Obtained absolutely negative CSF.

Evaulation:
October 1944

FIGURE 16.—*Serologic responses in tabes with primary optic atrophy. Note nonconcomitance of blood and spinal fluid*

Tabes dorsalis with primary optic atrophy

CASE #29, M. J., C., F., 29 years. 1935: STS positive routine examination. Previous treatment: 1939, 14 As., 36 Bi. 1943: Sudden diminution in vision (could see fingers only). O. D. 20/400, O. S. 20/300.

PENICILLIN 1,200,000 Oxford units intramuscularly in eight days

Days post-penicillin	Blood Kline units	Spinal fluid findings			
		Cells	Protein	Wassermann	Mastic
0	64	148	4+	4444	3331100000
9	64	16	3+	1244	2221100000
22	32	15	30 mg.	0012	2221000000
65	64	4	20	0122	1111000000
119	32	0	20	0011	1111000000
175	64	1	20	0011	2221000000
211	64	11	10	0000	1111110000

215 days postpenicillin: Vision 6/150 O. S., 4/150 O. D.—slight improvement.

FIGURE 17.—*Field changes paralleled with blood and spinal fluid responses in tabetic primary optic atrophy and sector defect due to chiasmal arachnoiditis or retrobulbar neuritis*

CASE #3, H. P., W., M., age 38, acquired syphilis. Primary optic atrophy in tabes, with euphoria, possible taboparesis. Fields show sector defect suggesting arachnoiditic or retrobulbar neuritic episode. Original spinal fluid—cells 122, Kolmer WR 4444, Pandy 4 plus, Mastic 4442110000, improved to cells 29, Kolmer WR 0123, Pandy 3 plus, Mastic 4432210000 by 2 Swift-Ellis treatments.

PENICILLIN 1,200,000 O. u.

Days post-penicillin	Quant. blood Kline units	Spinal fluid findings			
		Cells	Wassermann	Protein	Mastic
0	16	29	0123	3 +	44322100000
13		12	0012	2 +	2211000000
76	2	10	0112	1 +	3211000000

Began to lose ground visually, with slight confusion and increased euphoria

PENICILLIN 1,200,000 O. u. (retreatment)

104	16	11	0112	20 Mg.	2211100000
164	Less than 1	5	0012	20	2211000000

Definite improvement in fields, acuity and mental state. See second fields

250	2	2	0000	20	1110000000

Because of (1) low total dose (2,400,000 O. u. in 2 courses) and (2) persistent slight positive blood, despite normal fluid, a third course was advised, dosage to depend on eye and CSF findings

316	0	4	0112	10	3332100000

Note revival of slight abnormality of spinal fluid and negative blood, and compare third fields on 318th day, showing revival of old sector defect in right eye and new defect beginning in left eye, without recurrence of peripheral field shrinkage. Marked atrophy persists

PENICILLIN 4,000,000 O. u. (retreatment) given in 2 stages: 1,160,000 at 20,000 O. u and 2,840,000 at 50,000 O. u.

330	----------	3	0012	10	2221100000

For discussion, see next figure.

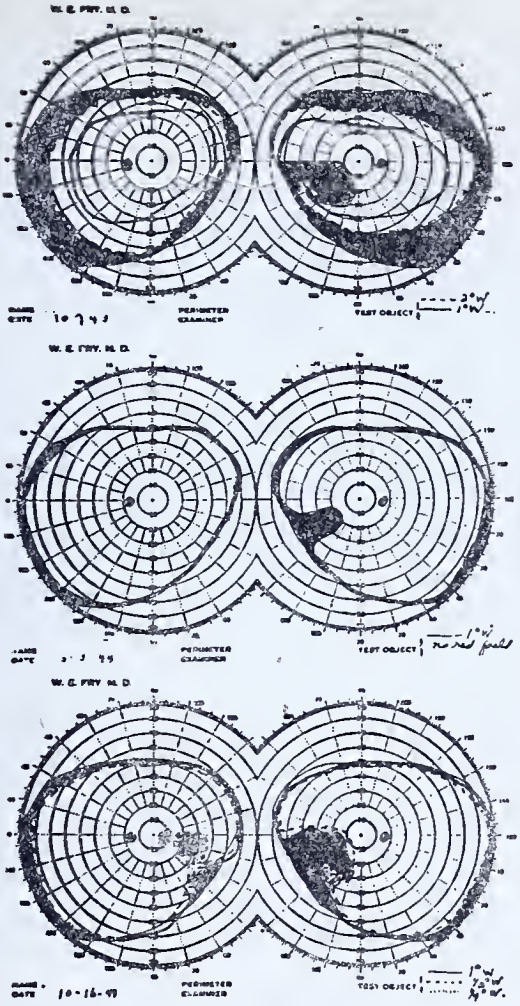


FIGURE 18.—*This patient (figure 17) has very slight improvement in field and has an unchanged (Dattner-Thomas inactive) spinal fluid after a third course of 4,000,000 O.u.—total 6,400,000 O.u.*

DISCUSSION OF CASE 3, OPTIC NEURITIS (?) WITH ATROPHY IN CNS SYPHILIS

The findings indicate:

(1) Improvement of blood titer; reversal of CSF to normal, improvement in eye findings under repeated "low" dosage courses of penicillin intramuscularly.

(2) Relapse (slight) in spinal fluid with such treatment (both first and second course).

(3) Relapse and extension of process (focal arachnoiditis, "island" type lesion?; retrobulbar neuritis?) after 2 courses of 1,200,000 O.u. each.

Focal lesions in the nervous system have long been known, depending on type and location, to resist systemic treatment and to progress independent of general serologic and clinical response. Penicillin produced both local and general response at low dosage. Will it block local and general recurrence, and progression, at the higher dosage? What is a nonsignificant spinal fluid abnormality?

FIGURE 19.—*The comparative lastingness of the good effect of penicillin here, remains to be determined. Retreatment at 2,400,000 O. u. should be considered*

TABES DORSALIS WITH PRIMARY OPTIC ATROPHY

CASE #12, J. L., W., M.,

SWIFT-ELLIS

14 treatments plus 34 Bi.; cerebrospinal fluid examination with each Swift-Ellis, as follows:

Days	Cells	Prot.	Wass.	Mastic
1	52	4+	4444	3444210000
8	10	4+	4444	5442211000
15	8	2+	1244	3332210000
27	6	1+	0124	2220000000
59	16	3+	1244	4442111000
75	12	3+	1124	4442210000
131	4	Neg.	0000	1110000000
144	3	Neg.	0000	0000000000
189	2	Neg.	0000	1110000000
202	2	35	Pos.	1112222000
216	2	Neg.	0000	1110000000
230	2	+—	0000	1111000000
250	3	+—	0000	1111000000
264	4	+—	0011	1111000000
395	2	Neg.	0000	1110000000

SWIFT-ELLIS STOPPED, FOLLOWED BY RELAPSE

583	58	4+	4444	2444310000
625	51	2+	1244	2443100000

PENICILLIN

1,200,000 O. u. begun 89 days after Swift-Ellis relapse was recognized. Spinal fluid findings follow:

Days	Cells	Prot.	Wass.	Mastic
0	74	4+	4444	3444210000
8	40	3+	1344	2443110000
43	10	2+	0124	1221000000
85	7	30	0011	1111110000
127	9	20	1122	1222100000
183	10	20	0011	1111100000
287	5	30	0000	1111100000

Pupillary reactions improved (2d case); optic atrophy unchanged; visual fields unchanged before and after penicillin.

AS MUCH WAS ACCOMPLISHED BY 1,200,000 O. u. PENICILLIN AS BY 14 SWIFT-ELLIS AND 34 Bi.

FIGURE 20.—*Return of a tabetic grade III spinal fluid (primary optic atrophy) to normal with 2 courses of 1,200,000 O. u. each*

TABES DORSALIS—PRIMARY OPTIC ATROPHY—AORTITIS

CASE #44, R. S., W., M., age 52. Routine STS positive in 1936. 1936–1941, more than 30 As. and 60 Bi.

Days post-penicillin	Blood Kline units	Spinal fluid findings				Remarks
		Cells	Protein	Wass.	Mastic	
PENICILLIN 1,200,000 Oxford units						
0	64	112	4 +	4444	2555410000	Postpenicillin grade II urticaria; angioneurotic edema hands and feet; duration 5 days; dermographism (not noted before).
20	64	34	30 mg.	1122	2233210000	
48	2	14	30	1244	2221100000	
63	16	6	30	4444	4442100000	
113	0.5	8	30	1124	2221100000	
PENICILLIN 1,200,000 Oxford units (retreatment begun 157 days postpen).						
232	32	4	20	0000	1111100000	Postpenicillin grade II urticaria; more marked angioneurotic edema hands and feet; duration 9 days; dermographism persists.

FIGURE 21.—*Response of lightning pains; nonresponse of Charcot joints*

TABES DORSALIS WITH LIGHTNING PAINS

9 CASES:

1,200,000 O. u., 1 course	1
2,400,000 O. u., 1 course	3
Retreatment totalling 2,400,000 to 8,000,000 O. u.	4
Lost	1

Worse	No change	Improvement				No data
		1	2	3	4	
0	1 1 R.	1 1 R.	2	2 1 R.	1 1 R.	1

OF 9 CASES, 6 SHOWED IMPROVEMENT

Slightly improved	3
Markedly improved	3

TABES DORSALIS WITH CHARCOT JOINTS

2 tabetics with Charcot joints, no improvement on 3,000,000 O. u. and 3,600,000 O. u. and 1 developed a second Charcot joint.

Evaluation:
October 1944

FIGURE 22.—*These results will for the moment bear comparison with those of fever therapy in paresis and taboparesis. The higher dosage seems the better*

R –Retreatment
DT–Dattner-Thomas normal

Paresis and taboparesis

LABORATORY RESULTS—27 CASES

SEROLOGIC TESTS FOR SYPHILIS					CEREBROSPINAL FLUID						
Relapse	Improv.	No lasting change	Worse	No data	No change	Relapse	Worse	Improv. (grade) 1	2	3	4
3	6 2 to Neg.	12 2 R.	5 1 R.	1	4 1 R.	2 1 DT.	2 1 DT.	2	8 2R. 1DT	7 2R	2
ONLY 6 OF 27 IMPROVED IN STS					UNFAVORABLE, 8 OF 27			Improved 19 of 27 Markedly improved 9 of 27			

CLINICAL AND SYMPTOMATIC RESULTS—24 CASES

	No change	Relapse	Worse	Improv. (grade) 1	2	3	4	Total	
	8 2 R.	0	1 1 R.	3	6 1R.	3 1R.	3	24	
1,200,000 O. u. penicillin	4	0	1	0	2	1	1	9	24
2,400,000 O. u. or over	4	0	0	3	4	2	2	15	
Observed over 200 days	2			2	1	2	1		
	Unfavorable—9			7		8		24	

15 of 24 clinically improved—8 markedly (grade 3 and 4). 8 observed over 200 days, 6 improved. 8 Given 1,200,000 O. u., of whom 3 improved. 16 Given 2,400,000 O. u., of whom 11 improved.

FIGURE 23.—*A striking clinical result, with serologic response, in taboparesis.*

CENTRAL NERVOUS SYSTEM SYPHILIS—TABOPARESIS

Case #70, H.M., W., F., age 47. In 1942 noted trouble in walking which became progressively worse, confining patient to bed. In 1943 began to have flight of ideas, with garrulous, slurring speech. Paranoid ideas were noted in addition, in 1944.

PENICILLIN 4,000,000 O.U. in 13 days.

Days Post Penicillin	Blood Kline Units	Spinal Fluid Findings			
		Prot.	Cells	Wass.	Mastic
3-16-44	[illegible]				
3-24-44 0	64		47 mg.	4444	4432210000
3-30-44 6					
[illegible] F. Marconi					
26	64	6	20	4444	4443310000
5-13-44 50	Helen L Marconi				
70	64	12	20	4444	5553211000
110	64	1	30	0012	2221100000
187	64	3	20	0112	2221000000
10-6-44 198	Helen L. Marconi				

ON THE 198TH DAY IMPROVEMENT HAD BEEN MAINTAINED, ESPECIALLY IN GAIT, WEIGHT, WRITING AND MENTALITY. Still some slurring of speech, and euphoria.

Notes

Patient could not write or do housework. Had auditory hallucinations, personality changes, disorientation, tremor of tongue, hands and mouth, slurred speech. On second day of penicillin therapy had Herxheimer reaction with right-sided convulsions becoming generalized. After 24 hours, penicillin reinstituted at half-dose to total 1,200,000 units, without untoward effect. By 16th day, completely oriented, memory, speech, tremor improved, electroencephalogram improved. In 4 months patient tremor-free, speech and writing normal, well oriented, hallucination-free, and satisfactorily performing housework including marketing with points and driving car.

FIGURE 24.—*Maintained improvement in spinal fluid in early taboparesis (meningovascular neurosyphilis?)*

EARLY TABOPARESIS

CASE #64, R. B., W., M., age 37. Questionable chancre 1925, routine STS 1942 positive, slight symptomatic changes. Received 22 mapharsen, 19 bismuth subsalicylate. Spinal fluid findings as below:

PENICILLIN 2,850,000 Oxford units—50,000 O. u. every 4 hours

Days post-penicillin	Blood Kline units	Spinal fluid findings			
		Cells	Protein	Wassermann	Mastic
0	0.5	72	40 mg.	4444	3555521000
22	Neg.	5	20	0011	1111000000
56	Neg.	5	20	0012	1111000000
98	Neg.	5	10	0000	1110000000
196	Neg.	4	20	0000	0000000000

Spinal fluid reduced to normal and maintained to 196th day.

As a general statement of the situation in a single sentence, we may say that penicillin, as sodium salt of *an as yet incompletely* analyzed and understood substance, is an effective therapeutic agent in the treatment of late syphilis. Under conditions not yet clearly defined, it produces transformations symptomatically and serologically without reaction, or even serious inconvenience to the patient, which are equal if not superior to those obtained by long and arduous procedures involving the arsenicals and heavy metals.

The status of penicillin in relation to fever therapy is not here examined or discussed, inasmuch as work in this field is still in its very beginnings. If penicillin continues to display the promise which we believe this interim report justifies, it will displace all of the older methods of treatment or give away to a combination of them in which much labor and time for the therapist, and stress and danger for the patient, will be eliminated. Only by an extension of the experimental field in the direction of a better understanding of penicillin itself, of arsenic-penicillin combinations, and penicillin-fever combinations, will a full evaluation be achieved.

The Chairman: The last paper in this symposium will be read by Dr. J. F. Mahoney, Chief of the Venereal Disease Research Laboratory, United States Marine Hospital, Staten Island, N. Y.

PENICILLIN IN THE TREATMENT OF GONORRHEA AND SYPHILIS

J. F. MAHONEY, *Medical Director,* R. C. ARNOLD, *Surgeon,*
and J. C. CUTLER, *Senior Assistant Surgeon,*
United States Public Health Service,
Venereal Disease Research Laboratory,
United States Marine Hospital, Staten Island, N. Y.

The usual connotations of the title would restrict the present paper to factual material concerned with the penicillin treatment of gonorrhea and syphilis. Because of the character of the present conference, the liberty will be taken to expand the theme to include certain inferences, bearing directly upon the public health aspects of these diseases, which appear to be reasonably warranted by the information assembled up to this time.

At the moment an atmosphere of doubt exists as to the role assignable to penicillin therapy in the program for control of gonorrhea and syphilis. This is accompanied by uncertainty as to the justification for making the radical alterations in the control mechanism which will be necessary to accommodate the therapy. The newness of the product itself and the very limited experience in its use bespeaks caution. Out of the past there come hosts of ghosts and shibboleths which had their origins at times when adequate methods of treatment were lacking. This history further bespeaks caution and counsels a postponement of any decisive action until such time as more complete information has accumulated, especially as regards syphilis.

On the other hand, the withholding of any agent free from major objection and having the potential capacity of reducing the incidence of any infectious disease constitutes an irreparable loss in time of national stress.

In the present report an effort will be made to review the available material with the object of determining the probable capability of penicillin to replace the therapies which are employed at present in the control program.

As regards gonorrhea, a hurried review of the present status of the disease as a public health problem may be desirable. It is generally agreed that the published statistical information in regard to incidence does not reflect the true picture. The peacetime incidence of the disease is not known. Military rates can, as a rule, be questioned because of the influence of the penalty provisions of the misconduct law. However, the military figures probably form a fairly accurate index as to the trends which are in effect in both military and civil populations. Information bearing upon military units located within the limits of the continental United States indicates that a marked decline in the incidence of the venereal group of diseases has taken place in the generation between World War I and the present mobilization. The inference that gonorrhea enjoyed a proportionate share in this decline is permissible as it accounts for approximately 80 percent of venereal infections.

If the decline is as large as indicated then surely great credit must be given to the influence of the sulfonamides. The use of these compounds represents the only event in recent years from which an epidemiologic impact of the magnitude displayed could have been expected. It must be admitted that during this period general measures directed toward the control of gonorrhea came into operation in practically all portions of the country, but these were not of sufficient intensity to have produced the far reaching effect at present observed. Furthermore, in the last analysis, practically all of the public health effort was based upon therapy utilizing one of the sulfonamides suggesting that without this group of compounds control of gonorrhea would not have made outstanding progress.

The generally favorable situation must be credited not so much to the over-all cure rates produced by the sulfonamide compounds, but rather to their ability to curtail the duration of the infectious period in the majority of the patients treated. This additional weight on the side of the defense probably has been responsible for setting in motion a progressive decline in incidence which is now becoming apparent. If allowed to continue without interference, it is predictable that the strains of N. gonorrhoeae which are susceptible to the sulfonamides would soon cease to be a factor in maintaining the biologic existence of the species while the so-called sulfonamide resistant strains would be fostered and would, ultimately, dominate the clinical picture. Fortunately, the making available of the antibiotic substance, penicillin, has rendered this eventuality of minor importance.

The actual efficacy of penicillin in the treatment of gonorrhea has been demonstrated by many workers and may be considered as having passed from the field of experimentation except insofar as further refinements in usage are concerned. All evidence supports the belief that the product represents the greatest single advance in therapy ever to be experienced in any disease. Serious drawbacks have not been encountered although the development

of resistant strains, as time goes on, is always a possibility. The principal problem remaining becomes one of adapting the therapy to serve best a public health need by extending its availability to the community level as rapidly and as completely as possible.

It seems to be obvious that the venereal disease clinic as it is constituted at this time will not meet the needs of the oncoming situation. As a rule, the clinic is very local in its sphere of influence and, in the majority of instances, does not reach above the dispensary level of the population. If the influence of penicillin is to be made fully apparent in the control of gonorrhea a more general instrument, one capable of serving all strata of the population, will be needed. As the conduct of penicillin treatment is relatively simple and does not require special training, the placing of the product at the disposal of the general medical profession, as a State service for the management of gonorrhea, appears to offer the greatest hope of reaching the general public in the shortest period of time. As an additional service of the State, it would be essential to make freely accessible such diagnostic laboratory procedures as would be of assistance to the general medical man in the recognition of the infection.

The broad coverage made possible by an instrument of the above type would have the distinct probability of fostering a new spiral of decline in the prevalance of gonorrhea or in augmenting the one now in motion; this, through the very effective medium of reducing the mathematical opportunity for transmission of the disease by curtailing the infectious period.

The intensification of all educational efforts should become an essential part of the program, as should also the use of the venereal disease clinic or the rapid treatment center idea for the management of problem patients. The carrying out of an elaborate proof of cure utilizing repeated culture studies probably will be found unprofitable and unnecessary. A follow-up system designed to detect the presence of a concomitantly acquired syphilis, the invasion of which has been altered by the penicillin therapy of gonorrhea, should be provided.

In considering the advisability of utilizing penicillin therapy in the control of syphilis only the clinical and laboratory material which has been assembled by the writers will be used. This is due entirely to the need for certain items of information which cannot be obtained readily from the published experiences of other groups working in the same field.

The data will be taken from the records of 63 patients, each with the confirmed diagnosis of early syphilis, who have been treated and observed through the posttreatment period in a uniform manner. For the sake of convenience the patients will be divided into the two broad groupings of primary and secondary syphilis. As the records disclose that clinical relapse becomes evident before the end of the fourth month only the records of patients who have completed 5 months of satisfactory observation will be utilized. The average posttreatment observation time for the entire group of 63 is 7½ months.

In the primary group the records of 40 patients can be used for study. There were some variations in the treatment schedules which were followed but these are not of particular importance in

the present analysis. In all instances there was a prompt disappearance of the causative organisms from the secretions and a rapid healing of the ulcerations. At the completion of the observation period the patients were distributed as follows:

Thirty-six (36) were free from evidence of syphilis and the results of all serologic tests for syphilis were negative.

Two (2) had undergone clinical relapse characterized by recurrent penile primary lesions.

In one (1) a serologic relapse developed after an initial favorable response, the serologic reactivity decreasing to a very low level then rapidly returning to the original intensity.

One (1) patient cannot be accurately classified at this time and, although considered to be following a favorable course, has not become serologically negative. This patient has been classed as doubtful.

In the group of 23 patients who have been classed as secondary syphilis the general picture is somewhat less favorable if the usual implications are given to the persistence of positive serologic reactions. From the clinical standpoint, all patients in the group experienced a prompt and complete recession of skin and mucous membrane lesions and of such constitutional symptoms as accompanied the invasive stage of the disease. At the completion of the observation period the distribution of the patients was as follows:

Ten (10) patients were free of evidence of the disease, and results of all serologic tests for syphilis were negative.

Three (3) cannot be accurately classified at this time but are considered to be progressing favorably. These are considered as doubtful.

Seven (7) are looked upon as treatment failures because of persistent positive serologic findings.

Three (3) have displayed clinical relapse of an infectious character.

In fairness, it should be recorded that 1 patient, following a period of 8 months of negative serology findings after treatment for a penile chancre, returned to observation with a lip chancre. At that time the regional lymph glands were enlarged and firm. Darkfield examination of secretions secured from the lesion was considered to be positive for Treponema pallidum. The patient has been retreated for the second infection and is practically seronegative at the present. The occurrence is looked upon as a reinfection and as a favorable response to the initial therapy.

From the public health standpoint and considering both groups of patients, interest centers in the fact that in all patients there was a prompt termination of the infectious stage of the disease and in the 5 instances of infectious relapse there was an equally prompt recession of lesions upon retreatment with a routine of penicillin therapy similar to the original.

The significance to be given to the group of patients who experienced prompt healing of all lesions but who failed to attain complete reversal of positive serologic reactions becomes important from both the public health and the clinical viewpoint. The members of this group did not display a tendency toward clinical relapse and must be looked upon as a minimal source of danger as agents of transmission. Although considered as treatment failures the public health purposes may have been as well served in this group as in the one where the members became completely negative to serologic tests. The clinical problem, as to whether these patients should be retreated promptly and vigorously, or allowed to remain under observation and retreated only in event of clinical relapse, must await the passage of time for solution.

The clinical observations give rise to the belief that penicillin, employed as in the present study, has the very definite ability to shorten the infectious period of early syphilis and that infectious relapse is not encountered with alarming frequency. Also, that the patients displaying the initial lesion only at the time of treatment, with or without accompanying positive serologic reactions, respond as a rule in a more satisfactory manner than do those in whom the disease has progressed to the secondary stage. As experience accumulates the impression is strengthened that a large proportion of early infections treated in the manner employed in the present group eventually will satisfy reasonable criteria of cure.

Along this line it may be well to stress again that syphilis is a chronic disease characterized, as a rule, by long periods of latency and recurring periods of clinical activity. Because of this chronicity any assumptions as to the effectiveness of a form of treatment will always be dangerous. The syphilis organism is adaptable and may be expected to develop an escape from any threat of extermination. The production of resistant strains is always a possibility and, without doubt, a small percentage of individuals will be encountered who do not respond to the therapy as favorably as do the majority. However, the deterring factors and the possibility of a mistaken judgment appear to be outweighed by the potential capacity of the therapy to curtail the infectious stage of the disease and thus reduce the opportunity for transmission.

If the full effect of this sterilizing capacity is to be brought to bear upon the problem of the control of syphilis, the concerted, prompt, and uniform action of health organizations will be essential. This type of action might well be responsible for setting in motion a decline in incidence which may reach a level far below any which could have been reasonably anticipated through continuation of the present control mechanism in which the principal burden is placed upon arsenic and bismuth therapy.

On the very plausible assumption that penicillin will be easily obtainable in the near future and at a price which will be conducive to liberal usage, the following additions or alterations in the general structure of the veneral disease control mechanism are presented for such consideration as may be warranted by the present state of knowledge.

As regards gonorrhea:

(a) That consideration be given to the making of penicillin available to any licensed practitioner of medicine for the treatment of gonococcic infections wherever found.

(b) That the laboratory facilities concerned with the diagnosis of the disease be made as efficient and as widely available as possible.

(c) That a renewed emphasis be placed upon the investigation of sources of infection.

(d) That posttreatment follow-up observations be concerned equally with the discovery of concomitantly acquired syphilis and the results of gonorrhea therapy.

As regards the control of syphilis, two plans appear to be optional. The first is the adoption of a passive role with deferment of all action until such time as the accumulated experience in peni-

cillin therapy is sufficient to supply answers to all questions. The second is based upon the assumption that preliminary studies have already progressed to a point at which practical deductions are warranted. These concern the ability of penicillin therapy to shorten the infectious period of early disease with consequent restriction of opportunity for transmission.

If full and early advantage is to be taken of this ability, certain alterations in the structure of the control machinery should be effected as a means of implementing the newer therapy. In this connection the following considerations are suggested:

(a) That arsenic and bismuth therapy in early syphilis be abandoned and a suitable routine of penicillin treatment be adopted in control work.

(b) That the practice of providing medical treatment for types of syphilis other than infectious or potentially infectious be abandoned.

(c) That all efforts, educational and otherwise, directed toward case finding in early syphilis be intensified.

(d) That hospital beds be provided at the community level for use in the treatment of early infections.

(e) That laboratory facilities concerned with the early diagnosis of syphilis be made as freely available as possible and be maintained at a high level of efficiency at all times.

(f) That general educational efforts be intensified in order that the less burdensome, less dangerous and more rapidly effective therapy may not lead to an undue disregard for the disease.

(g) That the major portion of the energy at present being expended in follow-up of treated patients be diverted to case finding of early infections.

The above program would serve to take an early advantage of penicillin therapy in the control of syphilis, and risks only that the inferences as to spirocheticidal action, which appear evident at this time, will be proved incorrect by future studies.

The Chairman: The discussion will be opened by **Dr. Paul A. O'Leary, of the Mayo Clinic.**

DISCUSSION

PAUL A. O'LEARY, M.D.,
Professor of Dermatology and Syphilology
Graduate School University of Minnesota,
Mayo Clinic, Rochester, Minn.

My apprasial of the value of penicillin has been limited primarily to patients with neurosyphilis. However, I have had the opportunity of observing some patients with other forms of the disease who have been treated with this remedy. Since September 1943, I have treated 70 patients with various manifestations of neurosyphilis, and of this group there are 49 who have been observed for periods varying from 4 to 14 months, while the remainder of the group have been lost sight of or have not been reexamined recently enough to admit of inclusion in this report. Of these 49 patients, 10 had asymptomatic neurosyphilis, 9 had the meningovascular type of the disease; there were 10 tabetics,

15 paretics, 1 case of spastic paraplegia, 2 with optic atrophy, 1 a congenital asymptomatic neurosyphilitic, and 1 patient with optic neuritis.

Variation in the percentage of penicillin in the ampule may account for some treatment failures.

We have been primarily interested in the significance of the blood levels of penicillin, so that in many of these patients we studied the blood levels following intravenous as well as intramuscular injection. Up to the moment, I have not been able to formulate any concrete opinion as to the superiority of one measure over the other. Neither have I been able to determine what level of blood concentration of penicillin, irrespective of the method of injection, is materially superior. The reactions have been conspicuously absent with the exception of one patient, a meningovascular neurosyphilitic, who was given intraspinal penicillin in the form of 50,000 units and who had convulsive attacks following each of two intraspinal treatments. He had not had convulsive seizures previously, nor has he had any since.

I have given malaria therapy in conjunction with penicillin in 19 of these 49 patients. The penicillin does not in any way inhibit the course of malaria, nor have I been able as yet to note any benefit from this particular combined form of treatment. It is much too early to attempt an evaluation of this system of treatment, but up to the moment the results seem to parallel those that follow a course of malaria when given alone.

Approximately one-half of the patients with clinical signs of neurosyphilis who received penicillin alone reported some improvement in their well-being. This was not constant but I have noted that those who derived a satisfactory serologic reversal to normal also derived considerable gain in weight, one patient gaining as much as 25 pounds in 6 months. They commented also on the fact that they were better, were some stronger, and from psychic reasons or otherwise believed that the penicillin made them feel better. I think this observation goes back to the days of tryparsamide as well as to the days of early malaria therapy. In other words, the improvement in the somatic complaints, I feel, has always had a favorable prognostic sign, preceding the serologic reversal perhaps by years. The serologic reversals of the blood or spinal fluid have not been so numerous nor have they been so encouraging to me as the clinical improvement. It seems that the amount of penicillin given is not the factor that alone determines the eventual outcome of treatment. In other words, favorable serologic reversal has followed the use of 1,000,000 units and failure has occurred following 10,000,000 units given in three courses. The duration of the syphilis, especially the duration of neurosyphilis, has been of considerably more prognostic significance; for example, the best results occurred in patients whose syphilis was of comparatively short periods, of essentially 3 years or less.

Strange as it may seem to some of you, the only two patients of this entire group who derived a complete spinal fluid serologic reversal to the negative received 1,000,000 units of penicillin intravenously and 20,000,000 units intraspinally. One was an asymptomatic and the other was a meningovascular neurosyphilitic, both of whom reverted to negative within periods of 6 and 7 months,

respectively. There have been no reversals of the serologic tests of the blood to negative in my small group of patients, although the quantitative titer in each case has been reduced. In other words, there has not been a parallelism between the serologic reversal of the blood and spinal fluid reversal. Practically every case displayed some reduction in the intensity of the spinal fluid findings, however. A reduction in the cell count was the outstanding finding, with decrease in the protein as the next most common change. The colloidal gold reductions were inconsistent while the flocculation and complement fixation tests of the spinal fluid, although frequently reduced, tended to maintain some degree of positivity.

I cannot but comment at this time on the effort to streamline the spinal fluid test. I have seen in several institutions lately a spinal fluid test that consisted of a flocculation on the spinal fluid, a cell count, and a protein estimation. The cell count was done anywhere from 2 to 3 days after the fluid was withdrawn, and I think in practically all of those cases it varied from 3 to 9 cells. Then when I was told that the 44000 complement fixation test on the spinal fluid was of no significance, I could see nothing but the protein left to evaluate the result. So I think that we must be a bit careful in tending to streamline, as I call it, our present spinal fluid examinations.

The influence on the subjective manifestations of tabes dorsalis in my experience has been slight. Leg pains were somewhat improved, but the gastric crisis continued as heretofore, and incontinence and ataxia remained unchanged. Of course, as anticipated there has been no change in the objective signs of the disease, such as pupillary reactions, deep reflexes, or sensory changes. However, the patients did note a sense of well-being and a gain in weight, both of which suggest to me that perhaps the future will produce more worth while changes than have been recorded thus far in this group.

The results in the patients with meningovascular neurosyphilis as a group were more encouraging than were the tabetics. In one patient ocular palsy disappeared; one patient with hemiplegia likewise regained approximately 75 percent of the use of her arm and leg. The results can be briefly summarized in that the patients felt better and were improving when last reexamined. However, the results in the patients who were given malaria and penicillin were better than those who received only penicillin.

The paretics who received only penicillin derived little or no benefit from 4,000,000 units or less, and I was not able to estimate the superiority of either an intramuscular or an intravenous technic in this particular group. As no improvement of a conspicuous nature had been noted in any of my patients from 4 to 6 months after they had undergone the course of penicillin, I found it necessary to give all of them a course of malaria, and I think in some the clinical improvement was a comparatively crisp reaction in contrast to the result we had received from the penicillin.

The patient with spastic paraplegia and the two patients with optic atrophy have as yet shown no material change, either good or bad, from the drug.

I have not had the opportunity of treating a patient with a

gummatous hepatitis, nor one with gastric phlebosis, so that my observations on the whole are pretty well-limited to the neurosyphilitic group.

I cannot close my comments without expressing a very favorable attitude toward the manner in which this study is being carried out. For those of us who went through the early days of tryparsamide and, subsequently, fever therapy, to have the opportunity of correlating and pooling our material in the manner that is now being done is to me a very marked advance in the progress of syphilis research.

The Chairman: We have a few minutes for further discussion of this very important topic. Will Brigadier General Hugh Morgan be willing to say a few words on the subject?

Brig. Gen. Hugh J. Morgan (Chief Consultant in Medicine, U. S. Army): I am extremely glad to be able to identify myself with this third meeting; it was my good fortune to attend the first and second conferences on venereal disease control. The program is less than 10 years old, I believe, and finds itself now in a position to gird up its loins for a new and more vigorous attack to gain its objective. It seems to me that the over-all program has become energized as a result of circumstances that have developed during this war and of the efficient, effective way in which the opportunity has been seized by the group that has been interested in it.

I think one of the most exciting chapters in medicine has been the development that has taken place, and the clinical investigation that has been carried out in the field of venereal diseases. Certainly we are at the beginning of what, in my judgment, is the last chapter of a history which has been written with travail and which has required an enormous amount of hope and industry.

I cannot take my seat without paying tribute to the leadership that this movement has been so fortunate to have. I am perfectly certain that the reason we have had 10 years of venereal disease control, and that we may look forward to another decade in which, in my humble opinion, the problem will be mastered is because we have had the leader to envision the problem, to organize the program, to implement it, and to carry it through. I am referring, of course, to Surgeon General Thomas Parran.

The Chairman: Whether you believe it or not, I did not coach General Morgan to make that speech. Thank you very much, General Morgan.

Is there further discussion? I see the Dean of Johns Hopkins Medical School, who had been a distinguished worker in the syphilis field until he became Dean; perhaps he has been able to continue some of his scientific work. Dr. Alan Chesney, would you have anything to say?

Dr. Alan Chesney: I don't think I can add anything to the discussion, except to compliment John Mahoney; I think he deserves a grand hand.

The Chairman: Dr. H. G. Irvine of Minneapolis, Minn.

Dr. H. G. Irvine: I should like to express my pleasure at being here and seeing Dr. Parran, with whom I had the pleasure of working soon after the first World War. I suppose there are not very many in the audience whose experience dates back to the last war in the venereal control program.

During the 25 years in which Minnesota has conducted its control program we have reduced our venereal disease prevalence to a point where early syphilis is almost unknown. It has been difficult to find sufficient teaching material for our university. We are faced now with a lot of old syphilis, and that is a problem that we have to think of for the future.

The problem of the follow-up work is not going to be reduced by rapid treatment. It seems to me that the benefits of follow-up work are more likely to accrue when the patient is in contact with the physician over rather a long period of time. My observation is that it is not possible for social workers to get patients to follow treatment. This must be a matter between doctor and patient, and if the doctor isn't interested, he isn't going to get anywhere with his patient. If he is interested, he must have a contact over a longer period of time than 7 or 8 days in the hospital to make any patient realize the seriousness of syphilis and the need of follow-up.

This point should be remembered in our consideration of the more than 4,000 cases treated in the rapid treatment centers over the country. Eighteen

percent of these cases were never seen after they left the hospital, two-thirds were not seen up to a year, and 85 percent were not seen up to 2 years. We thus have nearly 4,000 people wandering around for whom the possibility of cardiovascular syphilis or neurosyphilis is not known.

I can but express at least a word of warning against what may be untoward enthusiasm, especially from the public health viewpoint, toward the potentialities of penicillin.

I think we should plan to get the greatest benefit from penicillin treatment and rapid treatment centers. But I also think that we must emphasize the need for follow-up of these cases. Those of us who are not concerned primarily with research must continue to follow those methods whose final results have been proved, as well as the methods bringing quicker results in checking the spread of infection.

Some of the men here went through the period when salvarsan first came in. I saw some of the first injections of salvarsan in Vienna before it was brought to this country. I saw one dose given, and two doses, and so on, and over a period of 10 to 15 years all of us saw variations in the amount of treatment and the methods of treatment. For years those methods were judged on the basis of clearing up lesions and changing serologic reaction. Only after a considerable time did we realize this was not necessarily proving anything so far as the final effect of syphilis was concerned.

We must remember that many cases got well in those old days with only a dose or two of salvarsan or neosalvarsan; they did not all require 6 or 8 months of treatment. We must remember that many cases that were never treated at all finally got well. We must also remember that in some cases syphilis remained about the same in spite of all sorts of treatment. In other words, we must bear in mind the fact that certainty of final cure is in many respects just as important as reducing the spread by means of the present short treatments.

The Chairman: I see the city health officers of the two largest cities of the country present here. Dr. Stebbins, of New York City, have you any comment or discussion on this symposium?

Dr. Ernest Stebbins: I do not have any comment to make on the papers other than to say that as an administrative health officer I am very much excited about the whole presentation of the subject. I had the fortunate experience about a year and a half ago of having a visitor in my office, Dr. Mahoney, who came to us with some limited data which he said he very seriously hesitated to present to any scientific group. I was Secretary of the Epidemiology Section of the American Public Health Association at the time, and I felt that he had something important. While it was perfectly true, as he said, that it was far from proved, it was something that would be of interest to every health officer and venereal disease control officer in the country. He reported his very limited number of cases treated with penicillin, and none of us felt then that in so short a time we would have presented us such sound evidence of the value of this drug in the treatment of syphilis.

Health officers are anxious for the day when we can see wide use of penicillin in the treatment of both gonorrhea and syphilis.

The Chairman: Dr. Herman Bundesen of the city of Chicago? Dr. Bundesen declines.

Recess was taken.

The Chairman: We have two papers on the afternoon program on "Venereal Disease Control in the European Theater of Operations." We are very fortunate to have two medical officers of the Army who have just returned from that theater. The first speaker will be Colonel Donald M. Pillsbury of the Medical Corps, Army of the United States.

TREATMENT OF VENEREAL DISEASES IN THE EUROPEAN THEATER OF OPERATIONS

DONALD M. PILLSBURY, *Colonel, M. C.*,[3]
Army of the United States

The problem of the diagnosis and treatment of venereal disease

[3] Senior Consultant in Dermatology, Office of The Chief Surgeon, European Theater of Operations.

is one of increasing importance in the European Theater of Operations. At the end of hostilities, a very considerable proportion of soldiers who have acquired a venereal disease while in the Army will have received all or part of their treatment in this theater. The members of this conference will in the future have numerous occasions to judge the final adequacy of treatment of these patients individually, both before and after discharge of the patient from the Army. I shall attempt in this paper to outline the objectives of the program of diagnosis and treatment of venereal diseases in the European Theater, to indicate the progress which we believe has been made toward reaching these objectives, and to report certain variations in method which have been introduced. This report must necessarily be in summary, but it is hoped that sufficient detail is included to enable you, to whom we shall eventually refer our patients, to evaluate and criticize.

At the outset I should like to emphasize that these statements concerning the objectives in the treatment of venereal diseases are made with particular reference to their applicability to troops in the field, especially those in the combat zone. The professional care of soldiers in the European Theater of Operations, under the stimulus and guidance of the Chief Surgeon, Major General Paul R. Hawley, has reached a high level, and there has been no compromise on anything which has been needed to insure better health for the soldier. Nevertheless, it must be kept in mind that methods which may be applicable to practice in large civilian or fixed military hospitals sometimes, by reason of their cumbersomeness or toxicity or demands on laboratory facilities, prove inapplicable to troops in or near the line. No one can observe these troops, seeing even for a very short time the hardships, hazards, and inconveniences of their existence, and watching the difficulties under which their medical officers must work, without acquiring a determination that these men shall have the best that modern medicine can provide, and that research in military medicine shall be directed along lines most likely to furnish improvements in treatment applicable to them. Unnecessary laboratory work, needless complexities in treatment, and burdensome records, especially those designed to satisfy curiosity and not furnish information essential to the health of the soldier, must be critically examined. Military venereology has at times in the past been characterized by a stifling blanket of paper work, and any additional layer of reports in quadruplicate must be resisted on principle.

The general objectives of military venereology as it concerns diagnosis and treatment in a theater of operations may be stated as follows:

a. Prompt recognition, diagnosis, and reporting of venereal disease.

b. Early administration of treatment which will, with a minimum of toxic reactions, a minimum of hospitalization, and as little interference as possible with the duties of the soldier, produce noninfectiousness rapidly and afford the infected man the best possible chance of permanent cure.

c. Maintenance of records and application of such follow-up measures as may be necessary to protect the soldier against relapse or progression of his infection, both in the Army and in

collaboration with the proper agencies, after his discharge from the service.

The chief problems in diagnosis may be summarized briefly:

1. **Darkfield diagnosis of syphilis.**—Among military personnel, who have all been subjected to serologic screening and in whom over 95 percent of the syphilis encountered will be early, the diagnosis of the disease by darkfield examination acquires enormous importance. This audience need not be reminded of the crucial nature of this procedure. One is constantly reimpressed that it is at once one of the simplest and yet most difficult procedures in medicine. It is a method for the experienced, not the inexperienced, for clinically trained observers and not laboratory workers without clinical supervision or training. The following experience which was encountered in connection with the development of intensive arsenotherapy in the European Theater of Operations will suffice as an example.

Certain hospitals, originally 4, were selected to administer intensive arsenotherapy. Patients on whom a diagnosis of early syphilis had been made were transferred promptly to a designated hospital for treatment. If the diagnosis had been made at the referring hospital on the basis of a darkfield examination, it was always repeated at the General Hospital to which the patient was transferred. We were amazed to observe over a period of 8 months, in these 4 hospitals alone, some hundred patients in whom the finding of Treponema pallidum from an acceptable site reported by the referring laboratory, could not be confirmed by repeated examinations made during the following few days. To my best knowledge, only 2 of these patients later developed evidence of syphilis. This was a startling demonstration of the fallibility of the darkfield diagnosis of syphilis. The members of this audience are well-aware that mouth lesions are not suitable sites for obtaining material for darkfield examination for the spirochetes of syphilis, that the surfaces of dirty perianal lesions are hardly less hazardous, and that lymph nodes and dry secondary lesions are almost the only sites from which the organism can be obtained without the presence in the specimen of other more or less easily distinguishable spirillar organisms. However, this fact is not yet widely enough known, and constant reemphasis to medical and laboratory officers will prevent errors in diagnosis which, I feel sure, have been frequently made in the past.

2. **Diagnosis of syphilis on the basis of the STS.**—The wise clinician constantly suspects any laboratory in the performance of serologic tests for syphilis, to and beyond a point of absolute cruelty to the harried chiefs of laboratories. Constant pressure must be maintained to insure good technic and adequate cross-checking. The danger of biologic false positive reactions is now well-appreciated by medical officers, and it is believed that errors tend to occur chiefly on the side of conservatism, which is all to the good. The maintenance of good technics for the collection of spinal fluid specimens and for prevention of bacterial growth during transmission has been a source of continued difficulty in ETO. The addition of a suitable amount of merthiolate or, less preferably, of sulfanilamide, is at present overcoming this difficulty to a considerable extent.

With the introduction of intensive therapy in ETO, the quantitative Kahn test has been extensively employed in the European Theater, and medical officers are becoming increasingly familiar with its interpretation as a predictor of relapse. However, quantitative serologic tests have a considerable margin of error and minor variations in titer are of little or no significance, but confirmed marked increases in patients with early syphilis demand full investigation and attention.

3. **The diagnosis of gonorrhea.**—When adequate laboratory facilities are available, the diagnosis of gonorrhea on the basis of spreads and/or cultures is ordinarily done, although it is not required in ETO. Confirmation of the diagnosis of gonorrhea by spreads in patients with acute urethritis is by no means essential to the adequate treatment of such patients, and for those to whom laboratory facilities are not readily available, such a requirement may delay the administration of adequate treatment. However, in patients in whom the initial course of penicillin for gonorrhea is not successful, transfer to a hospital or venereal disease treatment center is arranged promptly, and complete study carried out. At the present time great emphasis is being laid on the importance of determining whether or not the soldier with gonorrhea has coincident early syphilis, before penicillin is given.

TREATMENT

I. Syphilis

a. It has long been apparent to syphilologists that, with prolonged methods of treatment, the benefits of arsphenamine and bismuth therapy were being applied to their full extent in only a small fraction of patients with syphilis who should receive them for the sake of the public health and their own welfare. Although subject to rigid control, military personnel often cannot be treated for syphilis regularly under conditions of global warfare. Rapid and repeated movements of troops, the difficulties of maintaining a clinical record which will remain with the patient week in and week out, and the varying availability of treatment facilities combine to produce significant and dangerous interruptions in the continuity of treatment. In ETO, a check of a representative series of syphilis registers some 18 months ago revealed that, in patients treated in the Zone of the Interior and various theaters of operations, including our own, only some 38 percent had received the 6 months of standard therapy in less than 8 months. It is not desired to belabor this point too much, but it must be kept in mind by all clinicians who will be called upon to evaluate the adequacy of treatment in these patients in the future. In this connection, rereading Padget's study of the 5- and 10-year follow-up results on the Johns Hopkins material, a study unique in the field, is recommended.

b. **Intensive arsenotherapy.**—In April 1943, intensive therapy for early syphilis was initiated in 4 General Hospitals in ETO. The experience with it, from the standpoint of toxicity and preliminary clinical results, proved satisfactory, and on Sept. 10, 1943, it was designated as the method of choice for all early syphilis occurring in ETO. Approximately 4,000 patients have received such therapy without mortality from treatment. Intensive arsenotherapy has now given way to penicillin therapy, and hence there is no occasion

at this time to recount our experience with intensive arsenotherapy in detail. However, since members of this conference will be called upon to evaluate the outcome of treatment in these patients in the future, the following abstract is taken from a paper by Courville, Wise, Myers, Crede, and myself, which will shortly appear in the British Journal of Venereal Diseases. Certain of our Allies have also employed this schedule of intensive arsenotherapy for syphilis:

(1) Period of treatment: Not less than 20 days.

(2) Technic: Multiple syringe. Continuous arsenoxide intravenous drip is almost impossible from a technical standpoint in large numbers of patients in military hospitals.

(3) Total dose of arsenoxide: 20 milligrams per kilogram of body weight. In individuals in whom treatment proceeded without significant reaction, this amount was given in 20 divided doses over a period of 20 days, i.e. a daily dose of one milligram per kilogram of body weight. A total dose of 1,500 milligrams of arsenoxide was rarely exceeded, regardless of the weight of the patient. Certain patients who had received less than 10 injections of arsenoxide on arrival in ETO were shifted to intensive therapy, and in such patients a total dose of 25 milligrams per kilogram of body weight, including that previously administered, was given.

(4) Bismuth: Coincident bismuth therapy was given, in the amount of 8 injections of 2 cc. each of a 10 percent suspension of bismuth salicylate during the 20-day period. During the initial months of this treatment, a considerable number of patients also received 10 weekly injections of bismuth after completion of the course of arsenotherapy, but such follow-up treatment was later largely discarded.

(5) Precautions during therapy: The successful experience with this type of intensive arsenotherapy as far as mortality from treatment is concerned may, it is believed, be attributed to two precautions which were employed. These were, first, that intensive arsenotherapy would be given only in hospitals approved by the Chief Surgeon and, second, that medical officers undertaking such therapy should receive training before undertaking it. The laboratory procedures advised during the course of such therapy were constantly lessened on the basis of increasing experience. One fact emerged strongly—that with a schedule of treatment in a period of 20 days, serious reactions almost never occurred in the absence of fever, and special laboratory studies were more and more restricted to patients showing a rise in temperature from the fifth day of treatment onward.

(6) Toxicity from treatment: A series of 775 patients treated in 4 General Hospitals between April and December 1943 was analyzed as follows:

Number of patients treated	775	
Number in whom treatment was completed	746	(96.3 percent)
Number in whom treatment was discontinued because of reactions	29	(3.7 percent)
Reactions of significance—secondary fever (6th to 15th day of treatment)	97	(12.5 percent)
Reactions necessitating discontinuance of therapy (the secondary reaction)		
Secondary fever	17	
Neutropenia	2	

Hepatitis	
Toxicodermal reaction	
Encephalopathy	
Other reactions:	
Primary fever over 101° F (per os)	17
Moderate to severe bismuth stomatitis	
Minor skin lesions without fever	
Neuritis or nephritis	

The most recent tabulation of follow-up serologic results which has been released is as of June 1944. These are as follows:

Serologic results, patients followed 6 months or longer after completion of intensive arsenotherapy.

	Total	Negative	Doubtful	Positive
Seronegative primary	205	204	1	0
Seropositive primary	169	159	3	7
Secondary	61	51	4	6
Total	435	414	8	13

Spinal fluid examinations 6 or more months after completion of intensive arsenotherapy

Initial diagnosis	Total	Positive	Negative
Seronegative primary	100	0	100
Seropositive primary	109	1	108
Secondary	27	1 (?)	26

It is concluded that the method of intensive therapy employed in this series of patients has a clear and decisive superiority over prolonged methods of treatment in regard to completion of the outlined therapy within the prescribed period of time. It has relieved the unit medical officer of much of the burden of management of syphilis on prolonged schedules of treatment. The chief disadvantages of intensive arsenotherapy are the greater incidence of serious reactions as compared to standard mapharsen–bismuth systems, and the necessity of initial hospitalization for a period varying from 25 to 30 days. The preliminary reports available would indicate that the follow-up results as to clinical and serologic relapse will be satisfactory, and that the incidence of asymptomatic neurosyphilis will be lower than that encountered after prolonged methods of treatment (under 1 percent).

c. **Penicillin therapy.**—Penicillin treatment of early syphilis has been the method of choice since June 26, 1944. The method employed has been the total of 2,400,000 units as recommended by the Surgeon General. The number of patients so treated has been considerable, and several advantages of this method of treatment are apparent: (1) It is, for all practical purposes, nontoxic; (2) it controls infectiousness rapidly, always; (3) it may be administered without hospital facilities other than those necessary for darkfield, serologic, and physical examinations, and the administration of penicillin. One relapse after 2,400,000 units has been observed thus far (October 1944).

II. Gonorrhea

It has become evident that gonorrhea is now a relatively simple therapeutic problem. In a series of 1,000 patients treated in ETO (results summarized by Robinson) cure was obtained by the intramuscular injection of a total of 100,000 units over a period of 10 to 15 hours, in slightly over 95 percent. At the present time, penicillin therapy is the initial treatment of choice for all gonorrhea in ETO. Considerable latitude is allowed in the schedule of ad-

ministration of the initial course of 100,000 units, and an increasing proportion of such cases is being treated on an outpatient status. There is no reason to take up hospital beds with such patients. If cure is not obtained by the initial course within a period of a week, it is advised that the patient then be admitted to a hospital, where careful study for complicating urologic conditions is carried out. A second course of 200,000 units is given. In the very patients who are not cured by this second course of penicillin, administration of a subsequent series totaling 500,000 units is advised. To date (October 1944), no instance of failure of anterior or posterior gonorrheal infection to be cured by this regimen has been reported. It is difficult to appreciate the enormity of this advance until one has experienced the administrational and medical difficulties of caring for the large residum of resistant gonorrhea which was encountered under sulfonamide and local therapy. Such men constituted a serious problem in military medicine and in discipline. This problem no longer exists.

III. Diagnosis and Treatment of VD in the Armies

Certain difficulties in the diagnosis and treatment of venereal diseases become accentuated by conditions obtaining in the combat zone. For various reasons which need not be outlined here, adequately trained personnel and sufficient technical facilities for the accurate and prompt diagnosis of venereal diseases are difficult to provide in hospitals in the Army zone which are receiving large numbers of surgical casualties.

On the basis of plans made some months prior to D-day, therefore, the following general scheme of management is being employed within the Army areas in ETO, and is, it is believed, resulting in greatly improved accuracy of diagnosis and effectiveness of treatment. All patients with penile ulcers, or with gonorrhea which has resisted an initial course of 100,000 units of penicillin, are evacuated immediately to a venereal disease treatment center, usually established in a convalescent hospital. This special treatment facility is staffed by a medical officer with experience and ability in the diagnosis and treatment of venereal diseases, and adequate laboratory facilities for diagnosis are maintained, using personnel detached from the Army Medical Laboratory. The standard of professional care in such patients is greatly superior to that which is afforded when the diagnosis and treatment of venereal disease, particularly of penile ulcers, is divided among a number of hospitals. Increase in the case load can readily be met because patients can be quartered in tents or barracks, and do not require, except in special instances, all the facilities of an Evacuation Station or General Hospital. It is needless to point out that the availability of penicillin therapy greatly increases the effectiveness of such an installation. With provision of personnel and facilities for accurate diagnosis, the standard of management of venereal diseases is in every respect comparable with the best afforded in civilian or fixed Army hospitals, and with much lessening of the patient load which must be carried by Field or Evacuation Hospitals, and with avoidance of the necessity of evacuating patients farther to the rear in the line of communications by reason of venereal diseases.

IV. Determination of Cure. Follow-up of Penicillin-treated Syphilis

With increasing use of short-term methods of treatment for syphilis, the necessity for better methods of follow-up has been brought into sharp focus in the European Theater of Operations. Adequate follow-up is an absolute and inescapable responsibility, especially when new and relatively less established methods of treatment are employed.

a. Complete dependence upon unit medical officers for the carrying out of follow-up serologic tests after completion of standard therapy, intensive arsenotherapy, or penicillin therapy, will not be successful. This is due to a number of factors entirely unrelated to the interest and energy of the medical officer: His duties and responsibilities are large and varied; he is expected to be conversant with a bewildering array of circular letters, bulletins and directives (some of which he may never have seen); regular access to medical records under field conditions may be difficult or impossible to maintain. He needs and deserves all the help that can be afforded from headquarters. Certain methods have been employed in ETO, in collaboration with the Medical Records Division, as follows:

(1) After completion of the cerebrospinal fluid and physical examinations and the blood Kahn test which is required when the standard 6-month therapy is finished, or after 6 months of observation following intensive arsenotherapy or penicillin therapy for syphilis, the syphilis register is sent to the Medical Records Division, Office of the Chief Surgeon, for review and safekeeping. It is there subjected to summarization and review to determine the adequacy of treatment. If treatment is inadequate or the result not satisfactory, or if a procedure essential for the protection of the patient has not been done, the register is returned to the unit with a request for the indicated examination or suggestions for further treatment. Registers which are satisfactory, but on which further follow-up serologic tests are required, are held for safekeeping, and requests for the tests are submitted to the Commanding Officer of the unit of the patient at the proper time. Registers of patients in whom the treatments and periods of observation for cure are adequate are immediately sent to The Surgeon General with recommendation for closure.

In general, 25 to 30 percent of registers are returned to the patients' units immediately for essential data or further treatment, 25 to 30 percent are held in the Medical Records Division for follow-up tests as they become due, and 40 to 50 percent are sent to the Office of The Surgeon General. Under such a system, it is to be emphasized that in one-fourth to one-third of the patients, a deficiency in laboratory studies or in treatment is corrected immediately rather than allowing the deficiency to persist until the register would be submitted for closure under the ordinary procedure. In addition, prompt information as to the current effectiveness of the management of venereal diseases in the Theater is available, and opportunity for acquainting medical officers with acceptable methods is afforded.

(2) An individual record of treatment form, to be carried by the patient, was introduced in the European Theater of Operations in March 1943. This has subsequently been replaced by Form 78a

issued by the Office of The Surgeon General. It is difficult to estimate accurately the success of such a form. It is my feeling that it falls short of expectations in influencing continuity of treatment or performance of follow-up examinations. However, it does give the intelligent and interested soldier an opportunity to obtain such treatment or follow-up studies and, on this basis alone, its continuance seems worth while.

(3) The names of all patients who have received penicillin therapy for syphilis in ETO are submitted monthly by the hospital concerned to the Office of the Chief Surgeon, ETO, and are there tabulated and carded according to months, for requests for follow-up serologic tests. At the proper time, a request for a quantitative Kahn is sent out through command channels. Considerable experience was gained with such a central follow-up system in connection with intensive arsenotherapy, and it is believed that it will enable us to protect men under our jurisdiction against undetected relapse, and also indicate promptly any significant incidence of failures from the schedule of treatment now in use.

(4) Preservation of the syphilis register:—From the standpoint of future evaluation of adequacy of treatment, nothing is more important to the soldier with syphilis than the preservation and safekeeping of his syphilis register. For this reason it has been the policy in ETO to keep these registers on file in the Office of the Chief Surgeon after the spinal fluid and other examinations have been done, even though further serologic tests may be necessary. Such a system is possible only in a Theater which is relatively compact and where communication lines are not too long. It will at times result in delay in the taking of serologic tests when the soldier in question cannot be located promptly, but has thus far proved of the greatest advantage in maintaining more adequate follow-up, and in preventing loss of a record of vital importance, the syphilis register.

There are many other problems concerning which we need information. The diagnosis of chancroid, for instance, is not satisfactory; it remains a waste basket group dependent on the establishment of findings ruling out other disease. More information is needed concerning the essential follow-up procedures after penicillin therapy of gonorrhea. Are elaborate tests of cure at all necessary? As yet we have not encountered any significant weight of evidence that they are.

A critical problem is the one which has arisen from the circumstance that, in the treatment of gonorrhea with penicillin, we are inevitably subjecting an unknown number of patients to the risk of temporary suppression of signs of a coincident early syphilis infection. It has been recommended that all patients with gonorrhea be subjected to a serologic test for syphilis 3 months after penicillin therapy. However, it remains to be seen whether or not this is adequate, and every precaution must be taken to insure that a significant number of patients do not slip through the net with undetected syphilis.

Colonel Sternberg has addressed this conference regarding the plans which the Army and the Public Health Service have made for the detection of venereal disease and determination of cure, and insurance of such further treatment as may be necessary in

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soldiers being discharged from the service. I believe the plan which has been evolved is workable. Certainly the protection of the soldier and the community against undetected or uncured venereal disease is an absolute obligation upon the military and civilian medical service of the country. It is my belief that most medical officers in foreign Theaters of Operation would be exceedingly loathe to employ an essentially experimental method of treatment for syphilis, such as penicillin, unless there was good assurance that our patients would be protected from possible treatment failures after they have passed from our control. To those of us who cut our syphilologic teeth, so to speak, in the two decades after World War I, the results of inadequate treatment and failures of follow-up in discharged soldiers were a disconcerting object lesson. The knowledge and facilities for the prevention of the tragedies of late syphilis are available. They must be applied.

It is hoped that this brief resume has indicated that the Army Medical Service in the European Theater of Operations is motivated by a keen determination that the standard of medical and surgical practice for the men for whose health we are responsible shall be the highest obtainable, and that methods of treatment of proved value shall be applied without delay. We are appreciative of and greatly dependent upon the efforts of investigators in the Zone of the Interior who have contributed so greatly toward the revolution in the therapy of venereal diseases which has occurred during the past 2 years. By the development of more effective and less toxic methods of treatment for the fighting soldier, a considerable increase in the efficiency of the Armies has been effected. This is a real contribution for which we in the armed services are profoundly grateful.

The Chairman: The subject will be continued by Lieutenant Colonel Paul Padget, of the Army of the United States.

U. S. ARMY EXPERIENCES IN VENEREAL DISEASE CONTROL IN THE EUROPEAN THEATER OF OPERATIONS

PAUL PADGET, *Lieutenant Colonel, M. C.,*
Army of the United States

As has been brought out in the previous discussion, the purpose of this conference is to consider ways and means for dealing with problems which will be presented by the venereal diseases in the difficult period which will follow the present war. I well remember that in the first draft of these remarks I wrote, "The problems which will be presented by the venereal diseases in the United States following the present war," but only a moment of consideration was required to see the fallacy of so narrowly limiting the concept. The venereal diseases will be, as they have always been, a world problem, and with the conditions which we may anticipate to obtain in the postwar world, with tremendous shiftings of large population groups and with travel between and intercourse among the various peoples of the world on a scale so far unprecedented, we may take for granted that the venereal disease problem will be international, and we in the United States may base our plans upon that concept.

Not the least important part of that concept is the fact that our soldiers returning from long tours of duty overseas will be something like entering aliens so far as disease problems are concerned. Please do not misunderstand me; I have no desire to enter into, much less become a partisan to one side or the other of the controversy initiated when Dorothy Parker suggested that the returning soldier will be, as the Reader's Digest put it, "a stranger." The social readjustment of the returning soldier is in itself a problem with which this conference might well concern itself, but in the narrower field which I choose to consider we must view the returning soldier as a new problem so far as the possibility of disease transmission is concerned. He has been in contact with an alien population for a long period, regardless of military control, has been exposed to the communicable diseases characteristic of those people, and has suffered them in proportion to their prevalence in that population. Among the large body of men who eventually will return to the United States from Europe there will be a number who have acquired a venereal disease. This fact and its possible significance to the public health of the people of the United States must be carefully considered.

It is this idea, therefore, which promoted the inclusion of the present discussion in the program of this conference. It was felt that the experiences which we have sustained in venereal disease control in the European Theater of Operations might be of interest to this conference for two reasons: (1) Because of the public health problem posed by the returning soldier, and (2) because perhaps in some small way the experiences which we encountered when a large body of soldiers was moved from the United States to the United Kingdom and eventually to Europe, may point toward the problems which may be encountered when that same body of soldiers retrace their steps.

The venereal disease control program in the European Theater of Operations (E.T.O.U.S.A., familiarly known as ETOUSA) got under way in the summer of 1942, and became a full-time venture in September of that year with my assignment as Venereal Disease Control Officer. Since that time, the program which has been developed represents the collaborative effort of many people to all of whom I should like, did time permit, to give due credit by name. As it is, they consider me as their spokesman, here to attempt briefly to give you a picture of the problems which we have encountered, the accomplishments we have achieved, and the failures we have suffered.

The loss of military manpower caused by the venereal diseases may be minimized in two ways: First by the prevention of infection, and second by the use of treatment methods which reduce loss of military effectiveness from those infections which have occurred. This essentially bicameral nature of the problem was recognized in ETOUSA; and in the organization of the Office of the Chief Surgeon the problems of treatment were assigned to the Division of Professional Services, while preventive measures were developed in the Division of Preventive Medicine. Without in the least attempting to discount the important contributions which have been made by new developments in treatment in reducing the manpower cost of the venereal diseases, this discussion will be devoted entirely

to preventive measures since only those activities have been within my province of activity.

From the beginning it was apparent that whereas any venereal disease control program is made up of the same five or six basic ingredients, the technic of application of these various elements must be adjusted to meet local conditions. This was illustrated at first by the contrast between our experiences in the United Kingdom and in the United States, and more recently has been thrown into sharper relief by the striking differences between conditions encountered in the United Kingdom and on the Continent of Europe.

Basically, a venereal disease control program deals with four elements: The susceptible population—in our special case the soldier in the United States Army; the infected population—made up of the group of promiscuous women, an unknown number of whom are infectious at a given moment; the number of sexual contacts which take place between the susceptible group and the potentially infectious, and the protective measures taken to reduce the risk of infection when exposure has occurred. There is frequently a tendency to overlook the simplicity of this concept and to become involved in detailed consideration of technics. In common with most, therefore, we have listed a series of steps which can be taken to reduce the number of venereal infections. These are to be classified basically as those which can be applied within the Army itself, and those which are to be applied essentially or entirely to the contact population.

In the first group an educational program, the encouragement of substitutive activities, the provision of materials and facilities for prophylaxis, and the command control of environment are the essentials. In the second group the two most fruitful attacks are the epidemiologic approach which serves many useful purposes in aiding to define the problem, but which directly seeks to detect and eliminate sources of infection in the contact population, and the repression of prostitution.

As we review these various avenues of approach, examination of what is meant by education will suffice to illustrate the necessity for developing a venereal disease control program with consideration of local problems. All too frequently we encounter the use of the term "education" without the slightest consideration of what it is that should be taught. Certainly the soldier should know the fundamentals of human anatomy, sex hygiene, and the nature of the venereal diseases. Beyond that point, information which is useful to him in a training camp in the United States may serve poorly indeed abroad. One illustration will suffice. So far as I know, nowhere in the United States Army in training in the United States has there been developed an educational program which brings out the fact that the segregation and licensure of prostitution does not provide a safeguard against venereal disease. As you all know, there is an impressive body of carefully collected evidence, much of which was gathered at great expense to the manpower of our own Army, which shows conclusively that licensed prostitution serves only to spread the venereal diseases. In spite of that, we have in ETOUSA a great many soldiers, who believe, with that childish faith with which the small boy believes that a horse hair

placed in a bottle of water will turn into a snake, that a licensed whore is a safe sexual partner.

You can see, therefore, why we have found it necessary to develop our own educational program.

Going on through the list of activities within the Army, you can well understand that in our theater of operations, particularly in those early days when shipping was at a premium, we found the provision of substitutive activities in, so to speak, the manner to which our soldiers had been accustomed, an extremely difficult task. Great tribute should be paid to the ingenuity and imagination displayed by many in creating recreational facilities out of sometimes literally nothing.

The command control of environment, while relatively easy to accomplish for a military organization on a post or in bivouac, sometimes became extremely difficult in the case of service troops quartered in relatively small groups, sometimes in immediate contact with the civilian population. The use, where indicated, of such standard measures as curfew, bed check, and area policing were sometimes of great effectiveness.

Our experiences with prophylaxis are most interesting. There was, of course, a considerable variation in education and training of the soldiers reaching us, depending on how long they had been in the Army before being shipped overseas, in what post they had had their basic training, and numerous other determining factors. In general, however, as they arrived in ETOUSA, soldiers were inculcated with the idea that a venereal exposure, especially with a professional prostitute, should be protected by a condom, and should be followed by station prophylaxis. In the United Kingdom, however, our soldiers encountered relatively few professional prostitutes. In some of the larger cities there were a few professionals about the cheaper pubs and dance halls, and the Piccadilly area in London was well known to all GI's for its professional prostitutes whom they euphemistically dubbed "Piccadilly Commandos." There were, however, few or no brothels as such, and the large majority of the sexual intercourse which took place was on a friendly and noncommercial basis. This had the immediate and readily discernible effect of markedly reducing the impetus to seek station prophylaxis. Coupled with this was the fact that with the shortage of housing, it was frequently difficult to find suitable quarters for the location of prophylactic stations, and because of the blackout it was practically impossible to mark a station in such a manner as to be easy to find. The summation of these factors had the result that in the United Kingdom there was a small use made of station prophylaxis. By contrast, condoms were extensively used and chemical pocket prophylactic kits were not infrequently employed.

The situation in France has been entirely different. The soldiers are all aware that professional prostitution flourishes and up to the present there has been a much more extensive use of station prophylaxis than was the case in the United Kingdom.

With all of these differences between the circumstances encountered within the Army itself as it moved from the United States to the United Kingdom, to the Continent of Europe, the most striking contrasts were in control activities which could be developed among the contact population.

At the time I left the United States something over 2 years ago, there was in full development recognition of the dual importance of the repression of prostitution and the epidemiologic investigation of sources of infection as venereal disease control measures. I understand that both of these lines of approach have been energetically pursued with a resulting favorable venereal disease situation in the United States Army within the continental United States.

We attempted to assist in development of similar activities in the United Kingdom. With regard to the repression of prostitution, British law and custom forbid the operation of brothels and this is observed with some diligence. So far as the activities of the individual prostitute are concerned, however, British tradition respects an individual prostitute as a free subject (as opposed to the organization of a brothel), and will interpose no interference with a streetwalker in the practice of her profession. There is in existence a statute enacted in 1828, which makes it a misdemeanor, punishable by a 40 shilling fine, to obstruct free passage in a public way, and this has been interpreted by the Metropolitan Police as involving the laying on of hands. From time to time, therefore, a prostitute who lays hands on her prospective customer, while accosting him in Piccadilly, is had up in Bow Street and fined 40 shillings. This has the interesting result, by the way, that virtually all of the professional prostitutes either carry a muff or wear a coat with high pockets so that while working the customer over thoroughly with the elbow, they actually have their hands immobilized and therefore technically are within the interpretation of the law.

In the autumn of 1942, the venereal disease program in effect among the civilian population of the United Kingdom rested almost entirely on the concept that if treatment for the venereal diseases was made free, readily accessible and secret, all those infected would recognize the fact of their infection, and would seek treatment. In some of the venereal disease clinics in London it was customary to suggest to a new patient that he bring his contact to the clinic on the next visit, but available information suggests that this was seldom consummated. Elsewhere, with a few exceptions (notably Leicester), there was no effort at all made to utilize the epidemiologic approach.

Surveying the situation, it became apparent that a contact investigation scheme was essential as a venereal disease control measure among our troops. The enactment of the British Defense Regulation 33B made it possible for us to obtain and transmit the necessary information concerning sex contacts, and the Chief Medical Officer of the Ministry of Health, Sir Wilson Jameson, gave our tentative plan enthusiastic approval and paved the way for arrangement with local Medical Officers of Health in the areas in which we had troops stationed. Eight U. S. Army nurses (regular members of the Army Nurse Corps) were selected as the field workers for the scheme by virtue of previous training and experience in public health nursing. There was nothing unique in the manner in which these nurses operated. They interviewed soldiers with venereal disease, got from them as much as could be obtained regarding the identity of their sexual contact or contacts, identified such of these women as was possible and presented them with a tactfully worded invitation to avail themselves of the services of

the nearest clinic of the local health authority. As is the case elsewhere, a fairly large number of soldiers were unable to give identifying information regarding their sex contacts. Twenty-three percent, however, were found to give completely identifying information and an additional 63 percent gave information which was either worth pursuing or at least was worth filing in a relevant data file in case additional information was given on the same contact by another soldier. Of this group, it was possible during the first year of the operation of the scheme to identify 64 percent of the women sought and so to bring to examination a total of 914 women. It is not without significance that of this total number of women who were brought to examination, only 6 percent were discharged as being free from venereal infection and at the same time less than 9 percent had sought medical care prior to being found by the operation of our scheme. Since, with only negligible exceptions, the women were ready and willing to report to a clinic when the possible need for examination was explained to them (and you understand, of course, that there was not the slightest hint of compulsion or coercion possible in the approach of our nurses to British subjects), it is notable that so small a percentage had availed themselves of the opportunity for examination prior to the visit of our nurses.

It is not possible to ascribe the relative success which we had with the venereal infections among our troops in the United Kingdom to any one type of activity, but it is notable that the greatest decrease in morbidity from the venereal infections took place in the areas in which the location of troops and the geography of the district made it possible for us to pursue these epidemiologic investigations with the greatest diligence.

You will understand that under the present circumstances the requirements of security forbid my disclosing publicly exact rates or morbidity experiences. I regret this because I feel, and could I show you the figures I am sure you would agree, that we have a right to be proud of the venereal disease rates which our troops experienced in the United Kingdom. In the summer of 1942 when our first troop concentration in the United Kingdom began, the venereal disease rate among our troops in the United Kingdom was essentially the same as that obtained for troops in training in the United States. During that autumn and particularly in the general slump which followed the setting off of the African expedition, the venereal disease rates rose to reach a peak just after the turn of the year, at which time the rate was conspicuously higher than in the United States. Since that time, however, the rate has progressively declined, at first rapidly, in the first 6 months of 1944 more slowly, but the downward trend up until D-day was consistent and sustained, to compare favorably, and frequently to our benefit, with rates for the troops remaining in the United States.

And then came June 6, 1944; assault troops landed at the base of the Cotentin peninsula and the invasion of Festung Europa was on. In England, we had been the guests of people who spoke a similar and frequently understandable language and from whom we differed in mores and social customs only in details. In France, we encountered an equally friendly nation—a nation in fact more given to being demonstrative about friendship than are the British—

but with a language which is strange to most of our soldiers, and manners and social customs which differ sometimes widely from our own. The differences are so great that in developing a venereal disease control program applicable to our troops in France, very little of our British experience could be employed. As you well know, the French recognize and license prostitution. All over France there are licensed brothels, sometimes of great splendour and magnificence. Streetwalkers are also licensed and interestingly enough, although a professional prostitute may elect to be either a streetwalker or a brothel inhabitant, she may not be licensed for both types of activity at the same time. Regulation requires that these women submit to examination at periodic intervals—usually twice weekly. This is customarily observed by the brothel inhabitants since the Madame is afraid of losing her license if she does not insist upon it. The streetwalkers, however, are not so diligent and usually stop in for examination only at just such intervals as they think will keep them from being in serious difficulties with the police in case, as frequently happens, they are picked up on some minor charge. These examinations are most perfunctory and as a matter of fact the best characterization of the entire procedure was given by a French medical officer in a position of great responsibility. He said, speaking of the system of examination of prostitutes, "If the doctor is good, the system is bad; if the doctor is poor, the system is dreadful; and we know what kind of doctors make their living off prostitutes."

During the occupation in all communities in which we had troops garrisoned, the enemy had taken over one or more of the local brothels and had operated them exclusively for the Wehrmacht. Among captured enemy documents, we found what would be called in our Army an S.O.P. (i.e. Standing Operating Procedure) for the creation and operation of brothels. This 17-page mimeographed circular is a masterpiece of completeness, including the details of the signs to be posted in each woman's room, warning the soldier that she is not necessarily safe. There was an elaborate procedure for gaining entrance. The German soldier reported to the prophylactic station which was always near and sometimes in the bordello, surrendered his dog tags and got a ticket, which with 3 Reichsmarks entitled him to admission to the brothel and service by one of the inmates. On this ticket was recorded the name of the house, the name of the girl who served him and the time of service. He returned with this to the prophylactic station, there received station prophylaxis, had that fact and the time of administration entered upon this same ticket, and got his dog tags back. Directions to the soldier on the ticket were to retain it for a minimum period of 3 months; but to what end is not quite clear, since if he did come down with a venereal disease he was transferred to the Russian front without further ado. In spite of this complicated ritual, the enemy had a disastrous time with venereal infections in his French garrison and in two areas in which we have captured complete records of the experience, the venereal disease rates were over 125 per 1,000 per year.

The fact that we would encounter this situation had been anticipated during the period of planning for the European operation,

and on May 2, 1944, there was published by Command of General Eisenhower, an ETOUSA directive which said, in part:

"The practice of prostitution is contrary to the best principles of public health and harmful to the health, morale and efficiency of troops. No member of this command will, directly or indirectly, condone prostitution, aid in or condone the establishment or maintenance of brothels, bordellos or similar establishments, or in any way supervise prostitutes in the practice of their profession or examine them for purposes of licensure or certification. Every member of this command will use all available measures to repress prostitution in areas in which troops of the command are quartered or through which they may pass."

Subsequently, other and more specific directives were issued concerning the use of off limits authority to implement the basic directive.

Many of the French were surprised when we did not take over and operate bordellos for our troops, and some expressed the not unexpected opinion that they thought us slightly mad for attempting to deprive our men of the soldier's inalienable right to be served by a professional whore. When convinced, however, that this was a matter of carefully studied policy on the part of the Supreme Command, and was bona fide, the French authorities offered unexpected assistance. On September 15, 1944, which was as soon as action could be taken by the provisional government, the Minister of the Interior addressed instructions to all of the prefects of police in France to take immediate and effective action toward the repression of clandestine prostitution, and to inform the keepers of licensed brothels to forbid American military personnel entry to their premises on penalty of being closed for violation.

The feasibility of this second step depended, of course, on the assumption that we would provide sufficient police and command control of our troops to prevent disorder in case soldiers attempted to force entry when barred from brothels to which others have free access. In large areas and with large concentrations of troops, this has been done most efficiently, and it is reflected in low rates for venereal disease acquired in those areas and by the troops stationed in them. In other areas, the local commander has been either unsympathetic to the plan, or unable to supply this type of cooperation to the French, who understandably will not act without assistance from us. Paris is wide open, and this is reflected by the fact that as this was written, the venereal disease rate among troops on duty in Paris was 37 times as great as that of the rest of the Armies, and that for the entire United States Army on the Continent, 62 percent of all of the venereal infections acquired in France came from the Paris area, in spite of the fact that only a small fraction of the troops had had access to Paris at all.

To complete the contrast is the situation with regard to the practicability of epidemiologic investigation. In the British experience, you will recall, we could get information worth following for epidemiologic study in 86 percent of cases. In France, however, only a negligible number of our soldiers who acquire a venereal disease are able to give useful information regarding the identity of their contact, and with the language difficulty, names and ad-

dresses which sound authentic all too often turn out to be wrong when an attempt is made to identify the named individual. In some places where there is a large body of troops more or less permanently stationed in a small community, it has been possible to gain some measure of success with the type of epidemiologic investigation used in the United Kingdom. In the large cities and especially in Paris, however, this method so far has been of little value.

It must not be concluded from what I have just said that we have accepted an attitude of defeatism. Far from it. I believe, and can from the record document this belief, that a well-rounded program of venereal disease control when pursued with intelligence and energy, cannot fail to be effective even under the most trying circumstances. There is no magic word, there is no secret formula, but the fullest exploitation possible under the circumstances of each of the several methods which are available for the attack cannot fail to produce results.

The final phase of this contrasting picture is just being written. We went from England, a friendly ally with essentially the same language and social customs, to France, an equally friendly ally, but with a different language and social customs. We are now entering enemy territory where the language and social customs again are different, and where the people are hostile. Just what will develop for the Army of Occupation remains to be seen. I know that you join me in hoping that these developments will be soon and, from the standpoint of my responsibilities in the European Theater of Operations, I can only hope that when hostilities do cease, we can evacuate our troops from France with the greatest possible speed.

THURSDAY EVENING SESSION

November 9, 1944

The meeting reconvened at 8:15 o'clock. Dr. Thomas Parran presided.

The Chairman: When this conference was planned, we thought of it as a U.S.A. conference. However, we were anxious to have with us our colleagues from the south and from Mexico, with whom we have been carrying out important cooperative activities along the border, and we were, of course, anxious to have our colleagues from Canada with whom we have been working so closely—especially Colonel Donald Williams, whom we claim as almost one-half on this side of the line. We then found that there were in the United States a number of medical officers from other United Nations whom we have been very glad to greet here this evening.

As most of you know, the progress of our agenda has been such that it was possible to have presented to you today two papers which were scheduled for this evening, and that gives us this whole evening to hear from our friends who represent the other United Nations.

I think it is appropriate to recall that action among the United Nations has been moving forward in many fields in addition to the strictly military fields. You recall the declarations from Moscow by our own Secretary of State, Mr. Hull, and the foreign ministers of the largest of the United Nations and the historic meeting in Teheran, participated in by Marshal Stalin, Mr. Churchill, and the President, preceded by conferences in Cairo in which Generalissimo Chiang Kai-shek also participated. There was the conference at Bretton Woods a few months ago, where the world monetary system of the future was outlined and agreed upon, and the more recent over-all meeting at Dumbarton Oaks where the world security organization was gestated, if not born, and at the moment there is in progress at Chicago a United Nations conference dealing with the postwar problems of civil aviation.

During this time of war the United Nations have not been unmindful of the human problems with which each of us individually and all of us collectively will be confronted when victory is won. To this meeting, representing as it does the public health workers of this country, I would recall that the first of all of the conferences among the United Nations was that conference called in the early spring of 1943 at Hot Springs, Va., to deal with problems of food and agriculture. The fundamental problem of food for the people, of human nutrition, was a dominant consideration in that meeting of diplomats, agricultural experts, nutritionists, and public health officers. Out of that conference came a unanimous report for an interim commission which has perfected a report, outlining a future world organization to deal essentially with problems of human nutrition and with the ways and means by which agriculture can adapt itself to meet the nutritional needs of the people.

Then there was the first meeting of the Council of the United Nations Relief and Rehabilitation Administration in Atlantic City just one year ago. Again the problems of health, of food, of epidemiologic control were of first concern. Ways and means were outlined by which the needs of the people, relief from suffering, control of epidemics, could be effectuated in each nation as it is liberated from enemy control. The UNRRA, however, is a temporary organization. The world organization concerned with food and agriculture will contribute much to public health, but it is not primarily a health organization.

Those of us who have been considering this problem realize that one of the important sectors of international action lies in the field of public health. This has been referred to in recent months by Mr. Raymond Fosdick, President of the Rockefeller Foundation. "Public health," says Mr. Fosdick, "is one of the rallying points of unity for international collaboration." So it seems appropriate this evening that we should devote this session to an important segment, namely, problems of venereal disease control in the larger area of public health on an international sphere.

If it is true—and I think all of us agree with Mr. Fosdick that it is true—that public health is a rallying point of unity for international collaboration, then the venereal diseases, world-wide in scope, large in their effects upon

the health status and the progress of nations, should be, shall I say, a nucleus in this rallying point, this area of unity for international collaboration.

I shall not attempt to present to you each of our guests, but shall leave it to the chief of each delegation to present the members of his delegation.

Our first speaker is one of the leading authorities in the world on problems of international health. For many years an official of the Health Section of the League of Nations, his work took him into many nations. Within the past month I asked him into how many nations of the world his duties with the League of Nations had taken him. He replied, "All but two." So I have the very great pleasure to introduce to you the representative of the Chief Medical Officer of the British Ministry of Health, Dr. Melville MacKenzie.

INTERNATIONAL CONTROL OF VENEREAL DISEASES IN THE POSTWAR PERIOD: WITH SPECIAL REFERENCE TO ENGLAND AND WALES

MELVILLE MACKENZIE, M.D.,
Principal Regional Medical Officer,
British Ministry of Health

I should like in the first place to apologize for the absence of Sir Wilson Jameson, Chief Medical Officer of the Ministry of Health. Sir Wilson asked me to express his sincere regret that owing to pressure of work he was unable to accept Surgeon General Parran's invitation to attend. He attaches great importance to this conference technically and particularly in the opportunity it offers for mutual help and the pooling of experience between our two countries. It is only by such collaboration and indeed coordination that we may hope to reach a maximum of efficiency in dealing with the problems of venereal disease in relation not only to military demobilization but also the vast and unprecedented movements involved in the return to their homes of many millions of displaced persons after the war.

As an instance of the size of these problems I might mention that we have information, which we believe to be accurate, that there are at present in Europe alone, apart from the Far East and apart from the armies and apart from prisoners of war, 30,000,000 civilians who are out of their normal homes. These people will all have to come back, and that alone will suggest to you the size of one of the problems with which we shall be faced.

In England and Wales the first effort at the control of venereal diseases was in 1864, when examination for infectious venereal disease of prostitutes in certain military centers was made compulsory. This was found to be of little avail and the law was repealed in 1866. The next step was in 1913 when a Royal Commission on Venereal Disease was set up, and as a result of legislation following that Commission, it was provided that arsenic drugs should be supplied freely to practitioners. It required all the authorities to set up treatment centers and to give instruction to the public in respect to venereal disease. The government paid 75 percent of the cost of these measures to local authorities. Shortly afterwards further legislation was passed forbidding anyone to treat venereal diseases except qualified practitioners and forbidding the advertisement of any remedies for venereal diseases.

In 1924 the Brussels Agreement for the provision of free treatment to seamen of all nationalities was signed, and in 1935 further

regulations laid down the qualifications of a venereal disease officer. His qualifications are definitely defined for the whole country by law.

By 1939, as a result of these measures, 187 free treatment centers—115 in voluntary hospitals—had been created in England and Wales, and there were 13 hostels for the care and rehabilitation of girls. There were also 99 approved laboratories for free examination of venereal disease specimens. All of these measures had a very notable degree of success. There is good evidence that the new cases of early syphilis dealt with at the centers in England and Wales in 1939 were less than one-third of those in 1920. Further evidence of the decline of syphilis is seen in the following:

1. Deaths of infants certified as due to syphilis fell from a peak of 2.03 per 1,000 live births in 1917 and 1.43 in 1921 to 0.20 in 1939.

2. Admissions to hospitals for syphilis in the services stationed at home fell thus: Navy, from 8.1 per 1,000 per annum in 1921 to 1.96 in 1936; Army from 9.8 in 1921 to 0.9 in 1937; Royal Air Force from 4.1 in 1921 to 0.7 in 1937.

3. As indicating that no great amount of syphilitic infection has been left untreated in rural areas even in 1941, the number of syphilitic infections in servicemen which occurred more than 10 miles from any treatment center was only about 60.

Thus the condition at the outbreak of the war was fairly satisfactory. Then came the war and with it very many factors which had profound effect on the incidence of syphilis.

To quote Colonel Harrison: "Venereal diseases are spread by promiscuity and this is promoted principally by absence from home with only remote possibilities of returning there; reaction from mental strain; boredom; the possession of money to burn; gold digging; indulgence in alcohol in dosage a little higher than is customary for the individual, and, in some societies, custom and example. We have in England multitudes of temporary exiles from their own homes, many of them receiving very high wages and amongst them, as also amongst our own nationals, are numbers who periodically undergo intense mental strain and excitement. We have also too many reckless, unstable girls who drink far too much and are determined to have a good time come what may."

It takes very little imagination to understand the very many factors operating in England at present. First of all there is the gypsy life of the shelters, and the fact that hundreds of thousands of individuals are removed from their homes into new areas where they are under no parental supervision in the factories. There has been, of course, a great breakup of family life owing to evacuation of the mothers, the women with children under 5, to the country. The difficulty of the almost complete absence of familial discipline, the stationing of many individuals in very many lonely places—all these have operated to increase the amount of venereal disease in the country

Prior to the outbreak of hostilities, when we realized that war might occur, through the medium of discussion with individual medical officers of health the attention of local authorities was drawn to the importance of strengthening their venereal disease machinery to meet the increased incidence which would be inevi-

table in the event of war. Subsequently we took the following steps:

1. Medical Departments of Services periodically transmit lists of places in each region with numbers of infections to medical officers of health.
2. Provision was made for continuation treatment of service men at civilian venereal disease treatment centers.
3. Seventy-five percent of the cost of additional treatment facilities made necessary by wartime conditions throughout England and Wales was met by the government.
4. Provision was made for special practitioner service, under consultant venereal diseases officers, in places too small to justify the setting up of a center.
5. Periodical reviews of each area were carried out in the light of service infections occurring there and recommendations made to increase facilities if these indicated the need for such.
6. Legislation was passed to bring under examination the contact that is impervious to persuasion.
7. Education of the public was intensified.

There are one or two of these steps that I should like to amplify a little; first of all, the provision of special practitioner services. One of the difficulties with which we were met was that large numbers of girls were being infected in very rural districts; the difficulty was that, the nearest clinic being in a market town, the girl would be recognized if she went there regularly for treatment, and so we found that there was a new section of the population that was being infected and was not getting treatment.

In order to meet the need for treatment in rural areas where the creation of a center would be uneconomical, arrangements were made by which local practitioners with certain qualifications, or after an approved course of training, were authorized to treat cases in their own surgeries, the fees being paid by the local authorities. Time does not allow me to give here the details of the conditions under which approval is given, but I shall be glad to make such information available to any member interested. Since this new arrangement, authorized in December 1940, came into force, 147 special practitioners have been enrolled in more than 79 areas in 13 counties, so that quite a fair amount of the deeply rural parts of England is covered.

With regard to the compulsory examination of contacts: In 1942 there was a modification in special circumstances of the system of voluntary attendance for treatment. Representations were received that venereal diseases were being spread by a small number of irresponsible persons who refused to attend voluntarily for treatment and that medical officers of health should be given power to require such persons to submit to examination and, if necessary, treatment. The government decided that compulsory powers should be taken to deal with these cases and to reinforce the established system of reliance on voluntary attendance for treatment. Accordingly, in November 1942, Regulation 33B was added to the Defense Regulations. I should just note that this is a regulation made under the Defense Regulations and not under the ordinary laws of the country. This regulation made it an offense for any person indicated as a source of their infection by at least two pa-

tients under treatment for venereal disease to refuse medical examination or, if necessary, treatment by a special practitioner after being required to do so by a medical officer of health of a county or county borough, or to cease treatment until certified as not suffering from the disease in a communicable form. Regulation 33B has to a certain degree fulfilled its ostensible object in bringing under control irresponsible individuals spreading venereal diseases amongst the services. It has also had the effect of bringing under treatment large numbers of contacts who have been persuaded as a result of their being mentioned by one individual only as a contact. Thus during 1943, 1,000 persons reported as sources of infection were persuaded to undergo examination and where necessary, treatment. In the same period it was found necessary to serve a formal notice compulsorily requiring examination in the case of 143 persons and prosecutions were instituted in 16 cases.

Concurrently, education of the public has been intensified. In 1943 the Minister of Health decided to try to break the taboo on the public mention of syphilis and gonorrhea, and so to dispel the atmosphere of ignorance and secrecy which for generations has favored the spread of the venereal diseases. The British Broadcasting Corporation gave their powerful support, and Sir Wilson Jameson broadcast a talk on Oct. 23. It proved a signal success and the national and provincial press cooperated wholeheartedly. This was followed by a debate in the House of Lords on the whole problem of venereal disease. It became evident generally that the serious nature of the problem was widely appreciated, and that most people recognized that public discussion was in itself a help towards its solution. Subsequently local authorities were urged to push their educational programs through every available medium, including the cinema and the radio. As an instance of these activities, I might mention that an American feature film dealing with the problem was shown in 300 cinemas and a short film pleading for the free and frank discussion of venereal disease questions was shown in every cinema in England and Wales under the auspices of the Ministry of Information.

In order that the campaign should not outdistance public opinion, the public's reactions were measured through the Wartime Social Survey. The first investigation gave the welcome result that 91 percent agreed with the principle of telling the public about venereal diseases; only 2 percent disagreed. Interesting evidence as to the value of the intense educational campaign and the publicity now being given to the subject is shown by two facts: (1) There has been a marked increase in the number of persons who have presented themselves at treatment centers for examination but have been found not to be infected. During 1941 the figure was 44.5 percent of the persons dealt with for the first time at centers whereas in 1943 the number was 60 percent. (2) The Central Council for Health Education, which assists local authorities in their propaganda work, answered more than 100,000 individual letters resulting from propaganda work done.

What is the present position in England and Wales as compared with that at the outbreak of war? Before proceeding to figures, I would emphasize the many factors which may operate in relation

to statistical evidence and the mistakes which may arise in drawing conclusions without taking such factors into full consideration. Transfers from center to center, return cases, absence of practitioners on service, special conditions in certain localities, change in the age constitution of a population as the result of enlistments into the services, the stage of the disease referred to, the different criteria by which directors of centers judge whether or not a patient has completed treatment, and many other points must be taken into account in attempting to draw conclusions from any detailed figures studied. One instance will illustrate this. In one seaport the number of cases of syphilis in 1942 was 11 times the prewar figure but, after deduction of the maritime and service cases, the number was but slightly above the prewar average.

The number of civilians with early syphilitic infection who attended treatment centers for the first time during 1943 was 9,642 as compared with 9,046 in 1942. With the addition of infections among members of the British Forces in this country, the increase in syphilis in 1943 was 6.9 percent over 1942 compared with an increase of 29.6 percent in 1942 over 1941, of 40 percent in 1941 over 1940, and of 21 percent in 1940 over 1939. Altogether new syphilitic infections under treatment in 1943 were more than twice as many as in 1939, but although the incidence rate was still increasing in 1943, the rate of increase has fallen sharply since 1941 in successive years—29.6 percent in 1942 and only 6.9 percent in 1943; so there has been a definite decrease in the ratio of increase.

For comparison the venereal disease infections in the British Army stationed at home during the war have been:

1940	8.75 per 1,000 per annum
1941	10.31 per 1,000 per annum
1942	11.53 per 1,000 per annum

The 1943 figures are not yet available, but gonorrhea and syphilis were 7.23, and with the addition of other venereal infections the rate is not expected to have exceeded 12.

With regard to gonorrhea amongst the civilian population, no figures are available, but are suggested indirectly to some extent by the ratio of gonorrhea to syphilis in the services. It is interesting to note that this ratio has altered considerably since 1939. In that year in the services the ratio was 8 or 9 cases of gonorrhea to 1 of syphilis, whereas in 1943 there were only about four times as many cases of gonorrhea as syphilis.

This then is the present position. With regard to the future, it is clear that the revolutionary changes resulting from the newest treatments of venereal diseases may well require a careful reconsideration of our existing machinery. It is obvious, too, that as more personnel become available a first step will be to widen and increase our present procedures.

Careful consideration is being given at the present time to the possibility of making venereal disease, or at any rate certain forms of it, reportable diseases. For this purpose a committee has been set up by the Medical Advisory Committee to study the advisability of introducing some form of compulsory notification in relation to venereal diseases. Notification may be general, applying to all the venereal diseases and to all patients, or partial, applying to certain diseases only—congenital syphilis, or to certain patients

only—defaulters. Similarly, it may be accompanied by provisions requiring examination or treatment of persons notified or of others associated with them, or it may be left to methods of persuasion to ensure examination and treatment after notification. Furthermore, notification itself may be carried out in one of two ways, either by full name and address or by code, followed by name and address in the event of default only.

With regard to general notification, the committee regarded it as premature at the time, March 1944, to introduce any system of general notification. The reasons for this were: (1) doubt as to whether the public at this stage seeks administrative action of the kind involved in a notification system; (2) the possibility that notification would lead to concealment even if done by code, and (3) the danger that notification might result in the migration of patients from the specialist clinic to the less expert practitioner.

With regard to partial notification, the committee considered defaulters, cases of congenital syphilis and special types of cases. In respect of defaulters, the committee had doubts as to the value of notification in view of the fact that defaulters do not appear to be in practice a large source of venereal infection. Moreover, such notification would only be of value if there was a fully developed system of social workers to follow up cases. Such a fully developed system is by no means available at the present time, and its creation should precede the introduction of notification of defaulters.

With regard to congenital syphilis, the committee regarded this as a reasonable and desirable proposal but was not satisfied that the elaborate legal and administrative machinery necessary would be justified by the results obtainable. The committee felt similarly with regard to special types of cases, such as the notification of positive Wassermann reactions to expectant mothers or blood donors or of gonococcic ophthalmia neonatorum or vulvovaginitis.

The whole matter is, however, still under careful consideration, with the knowledge that what may be undesirable and impracticable during the war may be desirable and possible later. With regard to the future in general, I should refer to the report of the Joint Committee on Venereal Diseases set up in 1943 and consisting of representatives of the British Services, the American and Canadian Armies, the Ministry of Health, the War Office, other government departments, and the metropolitan police. The findings of this committee and its recommendations are too voluminous to enter into in detail here, but I would draw your attention to two points which may guide our policy in the future:

1. The Joint Committee emphasized the fundamental importance of increasing educational work amongst all classes of the population, including those in the services, the factories, hostels, clubs, and schools, by such means as seem appropriate. Reference was also made to the importance of lectures to medical students and practitioners and it was urged that in the medical curriculum stress should be laid not only on diagnosis and treatment but on prevention. It was further recommended that the importance of making the fullest use of laboratory procedures be impressed upon medical practitioners, as part of the educational program, stress

being laid at the same time on the difficulties of technic and interpretation and the need for regarding a positive result in such tests only as indicating the need for further investigation. The committee also urged the desirability of establishing the custom of testing every pregnant woman's blood. To enable this to be done, it was realized that a considerable increase in laboratory facilities would be necessary, and the committee urged that this should be done as soon as practicable.

2. The Joint Committee urged that still more work should be done in connection with the tracing and follow-up of contacts. In England and Wales contacts are traced both by means of special personnel and through the medium of the contact slip given to each original patient if the latter would persuade the person from whom he thought he had contracted his disease or any whom he might have infected to go for examination.

The restrictions on the current availability of suitably trained personnel has necessarily limited at the moment the amount of visiting that can be done in connection with venereal disease, but as soon as practicable this work will be intensified. In this connection I should like to pay tribute to the degree of success attained by the arrangements which the American Army nurses are operating in certain areas of my country in cooperation with the local health authorities, under which selected public health nurses of the United States Army seek out contacts named by members of their forces, and by tactful and discreet approach secure examination and, if necessary, treatment.

I have briefly outlined the work done in England and Wales in connection with venereal disease prior to the war and given the results, the steps taken during the war, and the present position as regards the incidence, and I have mentioned the lines upon which we are now thinking, particularly with reference to notification, education, and contact tracing.

In conclusion I should like to express my indebtedness to Colonel L. W. Harrison, Adviser in Venereal Disease to the Ministry of Health, for his help in the preparation of this paper.

The Chairman: The next paper will be by our friend and neighbor, Lieutenant Colonel Donald H. Williams, and we shall be very glad to have him present the members of his delegation to us before he gives his paper.

Lt. Col. Donald H. Williams: Before thanking you, Dr. Parran and the conference, for the invitation to be present with you these interesting days, I should like to accept your suggestion that I present certain representatives who are on the platform this evening, and who have come from Canada. I should like to present three members of the Canadian armed forces; Commander J. L. Johnston, Commander C. M. Oaks, and Commander A. L. McKay. Next we have Dr. S. Stewart Murray, City Health Officer for Vancouver, British Columbia; Major W. C. Mooney, who is Director of Venereal Disease Control for British Columbia; Major John A. Leroux, Director of Venereal Disease Control for the Province of Ontario, and Major F. Pilcher, Division of Venereal Disease, Ontario, one of your own patriots, but one who has gone up to the unwashed in Canada.

INTERNATIONAL CONTROL OF VENEREAL DISEASES IN THE POSTWAR PERIOD: WITH SPECIAL REFERENCE TO CANADA

DONALD H. WILLIAMS, M.D., *Chief, Venereal Disease Control,*
Department of Welfare and National Health,
Ottawa, Canada

On behalf of the Honorable Brook Claxton, Minister of National Health and Welfare for Canada, and on behalf of the Canadian delegates, I should like to thank you very much for the privilege and honor of being with you again. It is just 2 years ago that I had the pleasure of representing Canada at this conference. A great deal has happened since then, and I feel that before very briefly outlining what has transpired in the 2 years since I was present here, I should take the opportunity of expressing a very deep and sincere debt of gratitude on behalf of Canada for the very great contribution that has been made to our program in Canada by various agencies and individuals in this neighboring nation. I know that we would not have had a venereal disease control program in Canada had you not had a Surgeon General Parran. As a matter of fact, before this week is out there will be launched in Canada an extensive national educational program, and at that time over a nation-wide hookup, General Parran will speak to the people of Canada.

We have obtained constantly a great deal of assistance from the United States Public Health Service. The aid and assistance of the Army and Navy in venereal disease control programs have been open to us both in a personal way and in an official way, and we owe a great deal to the two service venereal disease control programs upon which our programs have been largely based in the armed forces.

One has to mention also the great contribution given in the field of law enforcement as a result of assistance from the Social Protection Division of the Federal Security Agency. A great deal of help has been obtained; only 4 months ago, Mr. Eliot Ness and Mr. Michael Morrissey crossed to Canada and rendered conspicuous attention to our problem from the standpoint of law enforcement, and one thinks also of the American Social Hygiene Association which has helped a great deal. I wish to acknowledge at this time the great contribution that these agencies and individuals associated with them have made to the Canadian program.

Two years ago when I spoke to the conference there was no Canadian venereal disease control program. There was a little spotty venereal disease control going on in certain parts of Canada, but there was no Federal division of venereal disease control. There was not a single venereal disease control officer in any of the armed forces. Today there is a coordinated Federal venereal disease control program, involving the closest administrative and personal liaison between the Navy, the Army, the Air Force and the Federal Civilian Health Department. In 4 of Canada's 9 provinces the Army venereal disease control officer is also the civilian venereal disease control director. Now these facts will give you an idea of how this type of close liaison has resulted in relatively rapid progress in a short period of time.

There have been provided certain Federal grants-in-aid to the provinces that have assisted in provincial collaboration.

It was necessary to state to the members of Parliament and the House of Commons in Ottawa, the basis of the new national program. In giving thought and consideration to this, it was felt that in Canada it would be impossible to attack effectively the problem of venereal disease and its control without using the four principal forces in the community. So it was that Canada officially recognized a so-called four-sector front against venereal diseases, utilizing the community forces and their respective agencies and individuals under the headings of the Health Sector, the Welfare Sector, the Legal Sector, and the Moral Sector.

It was recognized that without aggressive action on each of the four sectors, we could not meet with success. It was recognized that we each had specific training, specific knowledge, and specific technics on our own sectors to push forward; that we had to move forward in a coordinated way; that we had to officially recognize the importance of the fighting on each respective sector. This four-sector approach, approved by a committee of the House of Commons and later at a national venereal disease control conference, was put forward to the people of Canada.

It gave us a broad basis of attack, and the popular enthusiasm for this all-embracing program was exceedingly gratifying. Every agency in Canada and every individual could quickly see himself lined up against venereal disease on one of these sectors. On the Health Sector, of course, one found doctors, nurses, health departments hospitals, and others associated with health services, using the weapons of modern medical science deftly and with carefully planned strategy. On the Welfare Sector one found official and private agencies with their personnel dealing with the important socioeconomic problems that are related to venereal disease. It gave recognition to the fact that venereal disease is rooted in social injustice, and that social security and all it means in its broadest sense would assist greatly in spelling the doom of venereal disease.

On the Legal Sector, the courts, the legal profession, and law enforcement agencies find their place, fighting the community conditions that facilitate the spread of venereal infection—the illegally operating, disease dispensing disorderly houses or bawdy houses, using the technic of suspension and cancellation of licenses of certain hotels, rooming houses and restaurants, and other places that facilitate the spread of disease.

And then on the moral front recognition was given the importance of the church and the home in fortifying individual character and in strengthening the ties of home and family life, emphasizing the importance of the sanctity of marriage and influencing in an important way the problems of human conduct. Regardless of how much we medical men attempt to squirm and to get away from it, the one epidemiologic fact that we are certain of is that promiscuous sexual contact spreads venereal disease. We must recognize that there is a strong force in our churches and our homes that can deal effectively on this particular sector.

On the health front we evolved a six-point strategy. Briefly it

consisted of health education, the provision of adequate treatment services, preferably the improvement of public treatment services; the suppression of treatment by the quack and charlatan; the protection of the home and family from hidden syphilis by premarital, prenatal, and confidential preemployment blood testing, and finally the important work of tracing contacts and bringing them under treatment. This strategy is moving, and is being adopted by health departments generally throughout Canada.

One of the most important specific steps that has been taken in Canada has been that of adopting and putting to use within the last 6 months the uniform national notification form that is used throughout Canada. This new form has given impetus to reporting and to the provision of data concerning contacts and the facilitation process. For the first time in the history of Canada, during the past month we have been receiving on the weekly summary of communicable diseases a breakdown of the incidence of weekly reported venereal infection, this new form thus throwing into prominence the relative importance of venereal infection in the realm of communicable disease control.

Canada is on the verge of tremendous changes in the field of social security, and almost every one of the particular phases now under consideration by the Canadian Government have their direct and indirect implications as far as venereal disease control is concerned. Two months ago Canada created a new Department of National Health and Welfare. Health and welfare—the broad problems of social security for the nation—were given the prestige of a single department, and a week ago two deputy ministers, one of Health and one of Welfare, were appointed.

One of the big tasks in the social security field in the Welfare Sector is the payment, starting the first of July 1945, of family children allowances to all children, to every child in Canada under the age of 16 as far as I know. This payment, which will involve a quarter of a billion dollars during wartime, is one of the first and one of the most generous children's allowance programs instituted anywhere, and it will have a very great effect upon venereal disease, in that it will influence certain socioeconomic conditions which are the breeding ground of venereal diseases.

Another major step that we are preparing to take in Canada is the implementation of health insurance. The House of Commons had before it at its last session the third draft of a health insurance bill that will bring planned health services to every citizen in Canada. Of importance to us is the fact that there is attached thereto provision for a million dollars a year for a period of at least 10 years for venereal disease control. This million dollars annually for 10 years, with expenditures now being provided, will mean that each year approximately 16 cents per capita will be spent on venereal disease control in Canada.

In closing I would like to look a little further afield and to think of international collaboration. If there is one thing that we have learned from this war, it is the fact that we are all individuals, interrelated regardless of national boundaries, and the personal welfare of each individual in each of our countries is of importance directly and indirectly to the personal welfare of each individual in every other country.

Another obvious fact is that when the war is over we will be in a world of great commotion. There will be great movement, and because of modern transportation, rapid movement. There will be movement of students, of tourists, and the nefarious movement of white slave traffic. We are planning for this in Canada and have definitely changed the emphasis on our education and propaganda to the importance of the turbulent postwar period from the standpoint of venereal disease control. To us it seems that the greatest danger to the homes and families of Canada lies in the 2 or 3 years after the war. There is a great tendency for us to let our burden drop with the end of the war and the advent of peace. It is important that we realize that with peace our duties and our responsibilities to our citizens and their homes increase. Venereal disease is a global pandemic; and if we are to attack it, we must attack it on an international collaborationist basis.

The Chairman: I have the very great pleasure of next presenting to you the representative of the Mexican Department of Health, with which, as most of you know, we have been carrying out very active collaborative efforts, especially along our border, Dr. Jaime Velarde Thome of Mexico City.

Dr. Velarde: Dr. Villela deeply regrets not being able to be here and sends his best wishes for a very successful conference. It is my privilege to present Dr. Villela's paper.

INTERNATIONAL CONTROL OF VENEREAL DISEASES IN THE POSTWAR PERIOD: WITH SPECIAL REFERENCE TO MEXICO

ENRIQUE VILLELA, M.D., *Director, Antivenereal Disease Campaign,* Mexico Federal Health Department

(Delivered by Jaime Velarde Thome, M.D.)

Up to the year 1920, the health activities connected with the control of venereal diseases were limited to the weekly inspection and the registration of prostitutes. Only in Mexico City and in some cities in the States was the isolation of a small number of infected women effected; they were given a feeble and brief treatment, incapable in itself of converting the infected case into an uninfected one, nor sufficient to prevent subsequent infectious relapses.

In 1920 the first antivenereal dispensary was founded in Mexico City. The success was immediate and the benefits so evident that before long a second dispensary of the same type was established. With complete justification, one can say that the founding of these first two dispensaries marks the beginning of a new health policy in Mexico in relation to the control of venereal diseases and initiates the campaign to combat these socially important diseases.

Little by little the number of dispensaries in the capital were increased, and in 1926, when the action of the Public Health Department was extended throughout the country, similar centers for treatment were established in the more populated areas.

There are now 60 specialized antivenereal dispensaries distributed in the principal cities of the Republic. In addition, there are 450 health centers in smaller communities and 130 in rural areas whose activities include the control of venereal diseases.

A central office, with a full-time specialized public health officer is responsible for the technical direction and supervision of all the

antivenereal activities. In Mexico City the hospital Morelos has for a long time been used solely for the isolation of infected cases; at the present time it is being reorganized for better effectiveness in its mission. In the States, facilities have been afforded by the local authorities for the isolation of some of the infectious cases.

Medicines are furnished free of charge, and the technics for the administration of treatments are based on the principles formulated by the Clinical Cooperative Group for syphilis, and those of the American Neisserian Medical Society for gonorrhea.

Each one of the antivenereal services adheres to the following objectives: (a) control of the cases in an infectious stage; (b) adequate treatment to prevent infectious recurrences; (c) prevention of congenital infections; (d) case-finding and case-holding activities, and (e) educational activities.

The main antivenereal disease dispensaries have the necessary equipment for microscopic examinations. During the last few years the darkfield examination has been emphatically insisted on and at the present time many dispensaries are performing it as a routine practice. The zone laboratory system, where samples of blood are sent to the various laboratories, is used for serologic examination.

More and more attention is being given the investigation of contacts. There is now a group of visiting public health nurses specialized in the control of venereal diseases. As this is a relatively new and recently initiated work, difficulties of various natures have been encountered, but as a whole the first results have been very promising and encourage going ahead with much enthusiasm until the success that is to be expected of this work has been attained.

The educational program, which is being intensified, is directed toward informing the general public of the venereal disease danger, making use of pamphlets and posters. An effort is being made to improve the sound and film equipment. In addition, the following procedure has been recommended as routine practice: At least once or twice a week a 5- to 10-minute talk should be given to the patients, when in the waiting room, on the various aspects of the venereal diseases.

With the cooperation of the National University, the National Association of Venereology, and the Mexican Society of Dermatology, the central office of the venereal disease campaign organizes annual courses for postgraduates and medical students.

Legislation: In 1940, the Federal District and Territories abolished the registration and weekly inspection of prostitutes. On that same date laws were set up in the Penal Code making punishable by law the conscious transmission of venereal diseases, the incitement to prostitution, the exhibition and exploitation of brothels, and businesses dedicated to prostitution, and for contributing to the delinquency of minors.

Several States of the Republic are adopting, within their jurisdictions, similar legal measures, and in this way we can say that a campaign for the repression of prostitution is on its way. In this country there is still a huge task ahead of us, as other States are being obstinate and continue attached to the policy of establishing regulations for prostitutes.

There is a Federal health law that comprises the following principles: Compulsory notification of cases by the private physicians; compulsory treatment; compulsory hospitalization in necessary cases; premarital examination; compulsory application of the Crede method to every newborn baby; the responsibility of the Federal, State, and municipal authorities, as well as the workers' unions, of cooperating with the campaign against venereal diseases and establishing clinics or contributing to their support.

International Cooperation: By reason of the emergency conditions developed with the war, a cooperative program was initiated in 1941 all along the Mexico-United States border to combat, intensively, the venereal diseases which were finding new and more favorable conditions for their dissemination. This program, under the auspices of the governments of both nations, has been working very successfully with an intimate, friendly, and mutual cooperation.

In Ciudad Juarez, Chihuahua, better results have been obtained because the municipal authorities effectively seconded our efforts in a program for the repression of prostitution, and in this way Ciudad Juarez is being a model and example for the rest of the Republic, including the capital.

One of the most satisfactory results of this international cooperative program has been attained through the amplification of the educational program.

Several well-selected groups of public health officers have been given scholarships by the Pan American Sanitary Bureau, to take specialized courses in the United States Public Health Service Medical Center in Hot Springs, Arkansas; others have gone to Johns Hopkins University, Baltimore; some laboratory technicians to the Research Laboratory for Venereal Disease Control, Staten Island, New York, and a group of public health nurses to the Nurses' School in San Antonio, Texas. The benefits derived from this splendid cooperation have already been seen, and the firm improvement of the work of the campaign is already evident.

Also in the field of technical publications there has been notable advancement, thanks to the bulletin "Informacion Sobre Enfermedades Venereas" and to the "Programa Minimo de Trabajo para Dispensarios Antivenereos," which are printed in Mexico, published by the Pan American Sanitary Bureau, and which are being distributed to all the Latin-American countries. We must also mention the educational propaganda in the popular form of posters and films, which have been furnished by the Pan American Sanitary Bureau.

Cooperation from Private Doctors: The laboratories of the Public Health Department grant, free of charge and without any restrictions whatsoever, the requests from private physicians to make laboratory examinations for the diagnosis of venereal diseases. We are justified in saying, on the other hand, that it has not been possible to obtain the full cooperation of the private physician in the notification of the venereal diseases, even though our efforts pursue that end.

National Association of Venereology: This medical group which primarily assembles physicians specialized on this subject matter, public health officers as well as private physicians, and which has

associate members in various parts of the country, cooperates enthusiastically in the venereal disease program and publishes bimonthly the "Archives Mexicanos de Venereo-sifilis y Dermatologia."

Training Center: Being convinced that one of the fundamental necessities in Mexico was competently trained personnel, a training center in the control of venereal diseases was established in Mexico City. It has as its main objective the basic training of the personnel employed in the antivenereal disease campaign of the Federal health department, the personnel of other Federal departments and institutions as well as private physicians.

The center includes a dispensary, a laboratory, and the training center. In addition to the routine training of personnel, the center will conduct, semiannually, a clinic inviting physicians and the allied professions for the purpose of demonstrating diagnostic procedures, treatment, and prophylactic measures, educational technics, and allied subjects. It is hoped that through this means they will become interested in the antivenereal disease program and obtain their cooperation.

From a panoramic viewpoint, such is the state of the organization of the antivenereal disease campaign in Mexico. What has been accomplished is infinitely small compared with the great part there is yet to be done, and in the future, greater efforts, constantly revised, with a firm and supported tenacity, will be necessary to progress in this long road. One can already foresee that the postwar conditions will favor an increase in venereal disease and danger will follow. The human masses now in the battlefronts or engaged in agricultural and industrial production will return to normal civilian life; there will also be the tide of inter-American tourists which will overflow the Pan American Highway and the airlines that will unite the countries with each other, and all this will permit the treponeme and gonococcus to pass very easily over any sanitary, custom and geographic barriers. Then, more than now, it will be indispensable to have the sincere cooperation of the nations, to safeguard those two beloved ideals, peace and health.

The Chairman: I am sure that some of you may be puzzled in looking at your programs to see the name of Dr. Raymond A. Vonderlehr listed on this international sector. In his capacity this evening he is the American cochairman of the Health Committee of the Pan American Caribbean Commission. During the course of the day, a number of the speakers have been generous enough to refer to my connection with the campaign for venereal disease control which is represented by this third national conference. I am sure that I am voicing the sentiments of all of you when I introduce Dr. Vonderlehr as the coarchitect, also the chief engineer and general manager of the American venereal disease control program.

Dr. R. A. Vonderlehr: There are with us this evening several representatives from the Caribbean countries. First is Dr. Ernesto Quintero, the Venereal Control Officer of Puerto Rico. If Dr. Roy A. Anduze is in the room, may I introduce him as the Venereal Disease Control Officer of the Virgin Islands? We also have with us Dr. Pedro Vargas-Rosado, Assistant Surgeon of the Public Health Service.

INTERNATIONAL CONTROL OF VENEREAL DISEASES IN THE POSTWAR PERIOD: WITH SPECIAL REFERENCE TO THE CARIBBEAN AREA

R. A. VONDERLEHR, *Medical Director,*
Director, District No. 6, United States Public Health Service and United States Medical Advisor, Anglo-American Caribbean Commission

The material progress which has been made in venereal disease control in the British Isles and the Scandinavian countries offers the strongest motive for this symposium. This statement is made advisedly because of handicaps which have presented themselves during the war. British and Scandinavian progress and partial solution of the Canadian and United States problems raise the question as to what postwar action lightly infected populations will take to protect themselves against people heavily infected with venereal disease. Will this protection be gained by restricting migration? Or will all countries meet the need by developing effective control programs?

Caribbean countries, although scattered over a fairly large area, have always had the advantage of readily available regional waterborne transportation. Indeed travel between islands of different sovereignties may often be accomplished by skiff. On a regional basis, therefore, restriction of migration is impractical and impossible. All of the Caribbean islands must control the venereal diseases or all will remain infected.

The problems relating to control are manifold. Generally they relate to public welfare measures and to social service. Specifically, they include the education of the public in venereal disease matters and the adoption by appropriate governmental agencies of sound methods for the control of irresponsible persons who are or may soon become infected.

PROBLEMS OF PUBLIC WELFARE AND SOCIAL SERVICE

These problems are numerous and relate to many of the phases of civilized human existence. Worthy of special mention are availability of natural resources, population, housing, and peculiar customs. Many of the Caribbean countries do not have sufficient natural resources to sustain the population. There is no great mineral wealth known in most of them, in some the land is not sufficiently fertile to sustain a moderate-sized population, and some fertile areas are so overpopulated that it is impossible to raise enough food. Unemployment and lack of legitimate entertainment when funds are at hand frequently result in an increased number of indiscriminate contacts.

Dense population is a great handicap to venereal disease control work on some islands. Very thickly populated areas are built up, industries are not developed sufficiently to sustain the population, the needs of the inhabitants cannot be met, and, as is the case in sparsely populated lands with less natural wealth, the women are often forced into promiscuous contacts to obtain food. Lack of opportunity to obtain articles of personal adornment, love of excitement and adventure by those in very drab environments, and the

influence of "third party interests," including friends and relatives, are factors conducive to clandestine and professional prostitution. The importance of the economic factor is obvious when it is recalled that few places in the Caribbean pay a domestic more than an average of $100 a year. Women in this group may if so inclined collect 15 to 20 times this amount as professional prostitutes.

A constituent of considerable importance contributing to the venereal disease problem is poor housing. Squatters rights in many of the countries make it possible to construct an abode for only a few dollars. In the slum areas even of some comparatively small towns as well as in the cities, it is common to see 5 or 6 people living in crude one room abodes, surrounded by debris, and built in groups over marsh or other wasteland. In these strata of society the biologic facts of life are learned by direct observation at a tender age, and before long the children begin experimentation of their own if they are not seduced earlier by some adult. In a group of Puerto Rican prostitutes, 64 percent had their first sex experience before 16 years of age, 44 percent obtained this experience by seduction and almost 40 percent were 16 years of age or less when they became professional prostitutes (*1*). One must not get the impression, however, that conditions of this kind are peculiar to Puerto Rico.

Customs differ somewhat in the several political units of which the Caribbean area is composed. This is natural when one considers the difference in political status. In most areas the woman has not attained the same political and social equality she has in the larger countries of the United Nations. Most men regard women as fair prey and it is noteworthy that in many places a man is not considered fully matured until he has acquired a legal or consensual wife and one or more concubines. Particularly pernicious as a cause of overpopulation is the system of common law marriage. Such "marriages" often take place so frequently that a designated man or woman is living with one or more spouses each year. Turnover is rapid; the birth rate excessive; the venereal diseases disseminate.

A characteristic of the Caribbean people which is understandable on a historical basis, but which presents many difficulties to the initiation of desirable reform, is their reluctance to accept changes in custom. With illiteracy high, many people continue the customs, good or bad, of their ancestors. And the most harmful customs are often adhered to with inflexible obtuseness.

Even the climate of the Caribbean contributes to the venereal disease attack rate. One insular governmental publication, commenting on the need for clothing, states that clothes are required in the area only to conform to social custom and to protect the body from the sun. While there is an inherent modesty among the more primitive of the islanders, the allure and languor of these lands are not fabulous in spite of the fact that one must disregard certain shortcomings in environmental sanitation. Sparse clothing, even though the sarong is not indigenous, plus the seductive characteristics of the Caribbean night, do not make it easier here to sublimate basic human appetites than in less intoxicating albeit more temperate zone.

PUBLIC HEALTH EDUCATION

These social and economic conditions create one of the greatest needs for effective public health education that exist anywhere. In many areas, there is no demand whatever for modern health service and an integrated venereal disease control program. In most others if a demand is created it is so feeble that it gets no further than entanglement with the first few archaic customs. No doubt the high illiteracy rate contributes greatly to the lack of public interest.

It is inconceivable that many parents in the Caribbean area would be capable of teaching their children correctly in matters relating to human reproduction. It is most deplorable that the church has not done so since many of the people are deeply religious and the church is their only source of information. Even secondary schools, when they exist, have not been active in teaching hygiene and human biology, and the burden falls upon the health departments which reach mostly the people who are mature adults and who as a rule have already had some venereal disease experience.

Once an effective health organization is created in this area, its first job will be to mold public opinion. In accomplishing this, all of the promotional devices known to business should be employed. The aim should be to achieve the following:

(1) Teach the people what the venereal diseases are, the damage they do, what treatment those people should get who are infected, and how the diseases may be prevented;

(2) That the control of venereal disease requires the appropriation of public funds and that such money must be translated into venereal disease control service as rapidly and as efficiently as possible. This need applies especially to the training of professional and technical personnel and their employment on a meritorious basis.

(3) Develop the proper relationship between the venereal disease control program and other reforms, especially public welfare, public education and social service.

(4) Point out the facts regarding healthy relationships between the sexes and particularly that there is no more need for the male to indulge in indiscriminate intercourse than for the female;

(5) That commercialized prostitution, because of the facility with which it creates easy opportunity for promiscuous sexual contact, is the most important single mode of spread of the venereal diseases;

(6) That control of prostitutes to insure freedom from disease is impossible on a practical scientific basis and that repression of prostitution is not a function of the health department, but primarily of the police and the judiciary;

(7) And, finally, that on a humanitarian basis the community and the nation is obligated to attempt the social and economic rehabilitation both of prostitutes and of promiscuous women, who because of lack of resources are potential prostitutes.

CONTACT LIMITATION AND CONTROL

It was established years ago that when in certain areas the number of persons infected with venereal disease who do not seek

treatment within a reasonable period exceeds the number of those who do get therapy, the disease is on the increase. The paucity of treatment centers in many parts of the Caribbean offers conclusive proof that syphilis and gonorrhea are not under control.

Once clinics are established there are two ways to limit the number of infected people failing to seek treatment. One is case finding of irresponsible or ignorant infected persons, and it is assumed that case finding in the Caribbean is as good in its treatment centers as in any other part of the world. The second method of limiting the number of untreated infected persons is to prevent as far as possible the sexual contact which causes the infection. This means an informed public which insists on rigid repression of prostitution, effective police work in closing houses of prostitution and preventing clandestine contacts, and prompt action by the courts to insure that the women and their exploiters are punished with dispatch. And further, insistence that these law enforcement procedures apply alike to healthy and infected prostitutes and exploiting racketeers.

I know of no Caribbean country which has established a program of contact limitation based on these modern concepts. Yet it can not be said that the plan is not applicable in tropical or Latin-American countries for our colleagues in Mexico have already refuted this argument.

Acting on the theory that an aroused public demands action, I wish to describe briefly the prostitution system in the Caribbean. Solicitation may take place anywhere, although more than half the meetings occur in bars, night clubs, and other similar places. Seventy percent of the prostitutes in Puerto Rico use such places for solicitation and in all of them alcoholic beverages are sold. Most prostitutes work alone although a few have procurers. The vice is, therefore, not as well organized a racket as it has been at times in the past in North America and in Europe. Once business negotiations have been completed the contact is made in cheap "hotels" in the same building as or near the place of solicitation. Clandestine prostitutes frequently use their houses for contact or a room in an ordinary dwelling rented for the purpose; many exposures are made in public parks, on beaches, or other out-of-door places. The "hotels" as a rule are more popular and are really houses of prostitution. It is noteworthy that each bed in the average hotel is used from 3 to 4 times a night. When the bar or night club is located in the hotel the owner derives an income which greatly exceeds that of any other racketeer in the field, and often this owner or his representative recruits new prostitutes for his hotel.

LIKELIHOOD OF SUCCESS IN CARIBBEAN

Keeping in mind the special welfare and social problems of the area, it is of some importance to review all of the facts in an attempt to prognosticate the likelihood of meeting with success in the control of the venereal diseases. In this connection, it may be well to review some experience which has been gained on one Caribbean island in recent months.

A group of several thousand men in the armed forces established a contact rate of 18,000 per 1,000 men per year. These con-

tacts were primarily with prostitutes, and special precautions were taken to insure that the men received a type of controlled prophylaxis just subsequent to intercourse. In a period of approximately one year 3 cases of gonorrhea developed on an average for each thousand contacts. This was a comparatively low gonorrhea rate, considering the great promiscuity of the sexual partners concerned, and this was probably due to the effectiveness of prophylaxis.

Applying the experience of these men in the armed forces to the civilian population of approximately 2,000,000, we find that there are about 700,000 unmarried persons over the age of 15 years. If we assume that these unmarried persons have the same contact experience on an average that the men of the armed forces had, and if gonorrhea occurs no more frequently, we find that approximately 37,000 persons on this island develop gonorrhea each year. This estimate appears conservative in view of the sexual habits of the people, which I have already described, and the failure of the civilian population to use chemical or mechanical prophylaxis.

It happens that this area is better organized to provide for the clinical management and control of the venereal diseases than are most of the Caribbean islands. Probably 90 percent of the patients with gonorrhea who seek treatment obtain this treatment from government operated clinics. Yet only 7,500 cases of gonorrhea are reported annually to this insular health department. No morbidity data are available from private sources of treatment.

Comparable figures indicating the attack rate-treatment ratio for syphilis are available but are not as striking as those for gonorrhea.

This evidence suggests that under the lax standards of sex behavior, with the rampant prostitution which exists, and with the extensive lack of public information regarding the venereal diseases, it may well be impossible to control the venereal diseases in the Caribbean as long as we are dependent on therapeutic measures for control. In all probability not even penicillin therapy, when it becomes freely available, will influence greatly the gonorrhea attack rate because the number of patients seeking treatment is small in comparison with the large number of persons infected.

If the venereal disease problem is to be met, therefore, in the Caribbean area it is essential that broad social and economic changes be established which will stop the exploitation of women and place a limitation on the number of indiscriminate sexual exposures. In few places does "the revolving door" whirl faster (*2*) than in the Caribbean, and too large a segment of the population supplies the rotary power.

To put a brake on the revolving door the people of each island must demand positive action. They must see that their legislative bodies pass appropriate laws and that these laws are translated into comprehensive venereal disease control service. Many of the legislative bodies of the United Nations made mistakes after the first World War which have cost in human lives far more than we are paying now to defeat the Axis. We, in the United Nations, hope that by maintaining a system of world-wide liberty and justice we can prevent the plague of future wars. But we know that by establishing and maintaining a world-wide service utilizing modern health, social, and welfare measures we can stop in the

Caribbean, as elsewhere, the pestilence of venereal disease for all time.

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The Chairman: Returning again to the east, across the Atlantic, all of us have been inspired by the accomplishments of our Scandinavian friends in the control of the venereal diseases. We had expected to have here this evening the Surgeon General of Norway, Dr. Karl Evang. I had the pleasure of a visit with him 2 weeks ago. A few days later he was reported to be in London. Last week he was reported to be in Stockholm, and this week in Moscow, and that accounts for his absence here this evening. He is very ably represented by one of his colleagues, Dr. Thorstein Guthe. I take great pleasure in presenting Dr. Guthe.

REGIONAL VENEREAL DISEASE CONTROL IN EUROPE

Postwar Problems of Syphilis from the Point of View of Maritime Nations

THORSTEIN GUTHE, M.D., *Assistant Surgeon General*,
Norwegian Public Health Service

The regional health organizations of America, the Far East, the Middle East, and Europe have not been planned as units of global structure and important international health problems have therefore suffered from lack of coordination and uniform application in many parts of the world.

The defense of populations against venereal disease forms a significant part of public health work throughout the world, and the importance of venereal disease control as part of international health obligations becomes more accentuated as rapid communications shorten distances and large armies of military and civilian personnel are on the move in allied and enemy lands. Wars create new public health problems. They do not solve preexisting ones. This is perhaps particularly true for venereal diseases; war has been the traditional vanguard of venereal disease epidemics.

A general increase of venereal disease was experienced during World War I in most European countries, including Scandinavia. The causes for this are manifold, and are rooted in profound changes of social and economic patterns in wartime, i.e. the movement of masses of people for military, industrial, and other purposes; the upset of everyday life of individuals; the dissolution and disorganization of normal family life and relations; the increase of promiscuity, professional and clandestine prostitution. Similar conditions are found also during postwar economic and political upheavals. Thus, a catastrophic increase in the incidence of venereal disease occurred in Germany from 1918 to 1921-1922 after demobilization of the armies in World War I. During the war itself the increase in Germany is reported to have been relatively slight.

Syphilis is generally considered a better indicator of the venereal disease status in a country than is gonorrhea. In some parts of Europe the reduction in syphilis to a disease of relatively limited importance was a significant achievement in the interwar period from 1919-1939. Thus, in Belgium syphilis declined by more than 80 percent from 1921-1927 (from 6,143 to 682 cases) and

similarly in Holland after 1925. In the Soviet Union important legislation in 1927 reportedly made possible a subsequent decline of 23 percent in primary and secondary syphilis from 1927 to 1929 (from 451,363 to 354,295 cases). In England and Wales syphilis declined by 46 percent from 1931 to 1939. In France the situation seems to have been more uncertain. The steady decline of venereal disease rates after World War I in the Scandinavian countries of Denmark, Norway, and Sweden to 10 to 20 cases per 100,000 inhabitants per year has largely been recognized as one of the classical

TABLE 1.—*Acquired syphilis*

	1919	1932–1935[1]
Denmark	527	21.3
Norway	360	15.0
Sweden	119	9.4

Incidence per 100,000 population.

[1] Average per year for the period.

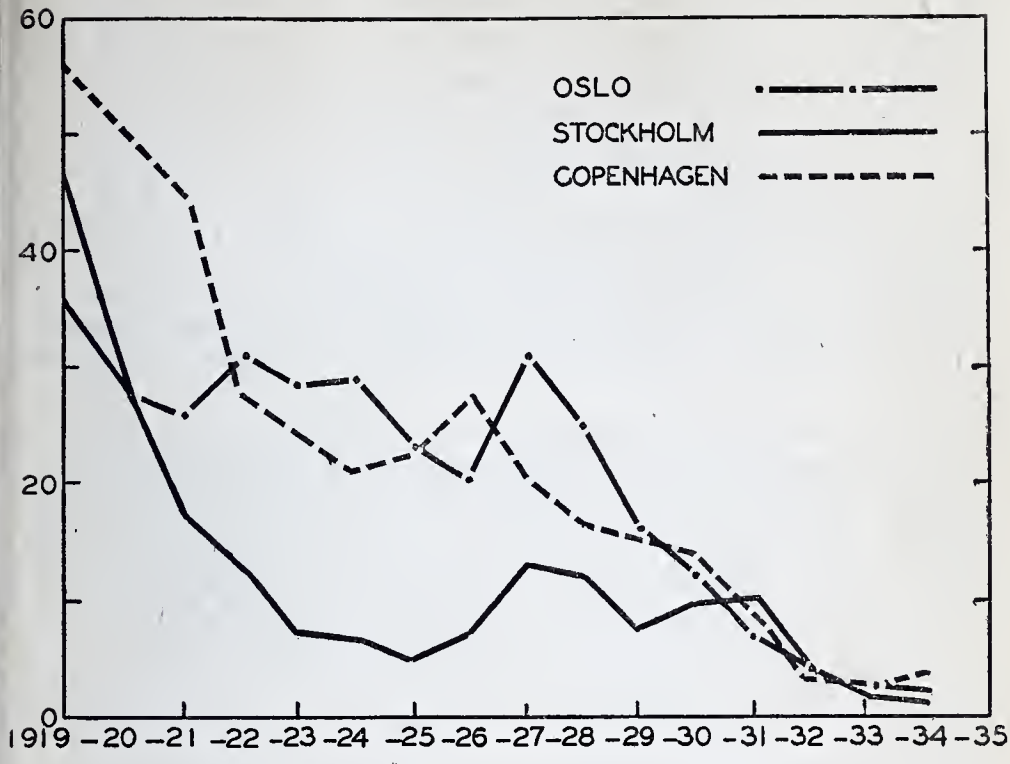
public health achievements in the field of venereal disease control. The statistics are well known, but it is pertinent again to emphasize the gains in this part of Europe.

This trend is perhaps best reflected in the statistics of the capitals in the Scandinavian countries from 1919 to 1934, where most of the cases occurred. The decline is illustrated in figure 1.

The incidence declined from about 55 per 10,000 in Copenhagen in 1919 to about 3.5 in 1937, and from about 45 in Stockholm to about 2, and in Oslo from about 35 in 1919 to about 5 per 10,000 in 1937.

It will be recalled that the New York City Commission of 1935 was appointed to investigate the prevention and control of venereal diseases in Scandinavia on the basis of these reported favorable results. For each of the 3 Scandinavian countries the Commission became convinced that the system of venereal disease notification and administration as a whole justified the conclusion that syphilis in Scandinavia had decreased in prevalence to a disease of limited importance. The means by which this was achieved have been described by the commission in their report (*1*):

FIGURE 1.—*Syphilis Trend per 10,000 Population, 1919–1934*



"Public Health measures for the control of syphilis and gonorrhea in all the Scandinavian countries are based on the principle that these diseases are communicable and should be dealt with as such. The law requires the reporting of cases, obligates patients to receive treatment, gives health authorities the power to enforce medical care including hospitalization if necessary, penalizes the knowing transmission of infection, and authorizes the finding and the bringing under control of all sources of infection and of all delinquent patients. While persuasion is usually successful, coercive measures are provided for that very small proportion of patients who are uncooperative."

Other important means were suppression of prostitution, emphasis on treatment and case holding, and financial responsibility for venereal disease cases by the State-guaranteed health insurance systems.

While the Scandinavian statistics point up the achievements in venereal disease control by long-term execution of antivenereal programs in one region of Europe, it should be remembered that there is a close similarity between the three Scandinavian countries with regard to living habits of the people, the organization of governments and administration of health problems. Illiteracy is practically nonexistent. Such similarities exist between few other peoples of Europe. As a matter of fact, the lack of homogeneity in populations may have contributed to the seriousness of the venereal disease problem in other parts of Europe in the interwar period, perhaps particularly in the Balkans.

In the southeastern part of Europe, that is, in Bulgaria and Yugo-

slavia, syphilis has been considered endemic for many years. In Bulgaria it is known that syphilis during World War I became increasingly frequent. At one time 14 percent of the soldiers of the army had syphilis and 21 percent had gonorrhea. In Yugoslavia 4 percent of the population of Bosnia and Hertzegowina had syphilis. In 1938 there were 453 cases of new syphilis per 100,000 population. The venereal disease problem in Rumania was serious during the first World War, due to continuous movements of population and armies. From 1921 to 1927 the average number of syphilitics represented 6 to 8 percent of the population in one region. In the tobacco regions it ranged as high as 23.2 percent. In Hungary in 1928, 54,079 persons were under treatment for venereal diseases. Of these, 310 per 100,000 population were under treatment for syphilis.

In these and other European countries where venereal diseases remained a matter of concern, notification of venereal diseases was unreliable and defective. In several countries venereal disease is still not reportable. Even in Belgium and France syphilis became reportable first in 1942 and 1943. Some countries in southeastern Europe passed adequate laws in the interwar period, but were unable to enforce them. Other countries lacked the public health and welfare means to carry through the programs. Thus, in a census of venereal diseases in Rumania in 1938 only 11.6 percent (21,326) of the recorded total of syphilitics (182,482) received treatment.

A great difference in the prevalence of syphilis was thus present in the northwestern and in the southeastern parts of Europe before World War II, and it would, indeed, be deceptive to evaluate European venereal disease problems as a whole from the standards attained in the Scandinavian countries.

The factors creating problems of venereal disease in wartime became recognizable in some European countries early in World War II. In England in 1940 patients receiving first treatments for syphilis increased by 12.5 percent. The total increase in syphilis among civilians and in the armed forces from 1939 to 1941 was 70 percent. In the Netherlands mortality from congenital syphilis increased by 39.5 percent from 1940 to 1942 (from 215 to 540 cases). In Belgium new cases of syphilis increased from 1942 to 1944 by 40 percent (from 1,796 cases in 1942 to 2,538 in 1943, and to 1,526 during 6 months of 1944). In France there are indications from the dispensaries that new cases of syphilis have doubled from 1941 to 1942 and doubled again from 1942 to 1943. In Germany likewise have come important indications of rising incidence of venereal disease. While the syphilis rate was 23 per 100,000 in 1938, it was 43 per 100,000 in 1940, and deaths from congenital syphilis in the larger German cities increased by 73 percent from 1941 to 1942.

While little information has been available from central and southeastern Europe during World War II, fairly complete data are available for Scandinavia. Some information is also available on Finland during that country's alliance with Germany. Scandinavian countries are the only ones in Europe which have had an efficient system of venereal disease reporting over a long period of time, and the venereal disease situation in occupied Norway and

Denmark, in neutral Sweden and in Finland might, therefore, be representative in determining the extent of the increase during the war in Europe as a whole, with a view to evaluating the magnitude of future antivenereal work in that region of the world.

TABLE 2.—*Syphilis 1932–1943*

	Prewar		War increase	
	1932–1935	1936–1939	1940–1943	Percent
Norway	15.0	13.3	33.7	153
Denmark	21.3	16.7	25.0	49

Average number of cases per year for the periods per 100,000 population

The steady reduction of syphilis (figure 1 and table 1) in Scandinavia continued until 1940 when Germany attacked Denmark and Norway. In both these countries a rise began in 1941. This rise continued into 1944. In table 2 the average yearly incidence for the 4-year period 1940-1943 is compared to the incidence for 1932-1935 and 1936-1939.

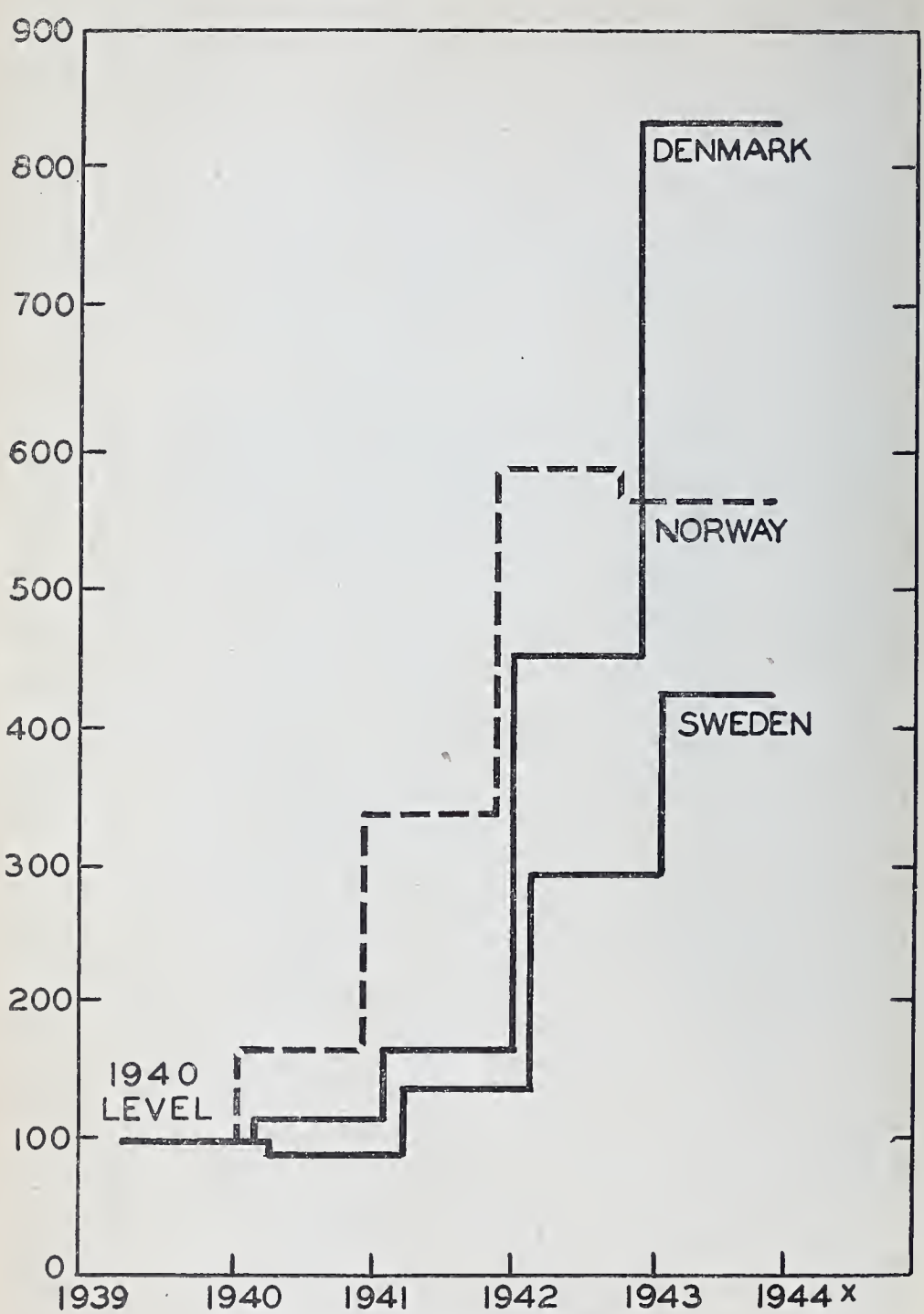
By using the 1939-1940 level of syphilis in the Scandinavian countries as a base index, the increase during the war from 1940-1944 is illustrated in figure 2.

It will be noted that the rise became accentuated in Denmark and Norway in 1942 and 1943 with 6.2 times more syphilis in Norway in 1943 (64.5 per 100,000) than in 1940 (10.2 per 100,000), and 4.8 times in Denmark (61.3 per 100,000 in 1943; 12.7 per 100,000 in 1940). In Denmark the rise continued sharply in 1944 (113 per 100,000), while in Norway the level was somewhat lower than in 1943. The computation for 1944 is based on the assumption that the incidence would be the same during the second half of the year as for the first, for which information is available. The increase from 1940 to 1944 is found to be sixfold in Norway and ninefold in Denmark. Both countries were invaded at the same time. Conditions in occupied Norway, however, are generally considered to have been more severe than in Denmark during the first years of occupation. This may be due in part to greater forced movements of population groups and the presence of a greater number of Germans per 1,000 civilians than in any other country in Europe. The possibility that the general trend of events is reflected in the trend of syphilis incidence must be considered.

In neutral Sweden the rise began in 1942 and seems to be continuing. Neutral Sweden has enjoyed considerable wartime financial prosperity, and this may have been a contributory cause for the rise of venereal disease in that neutral country.

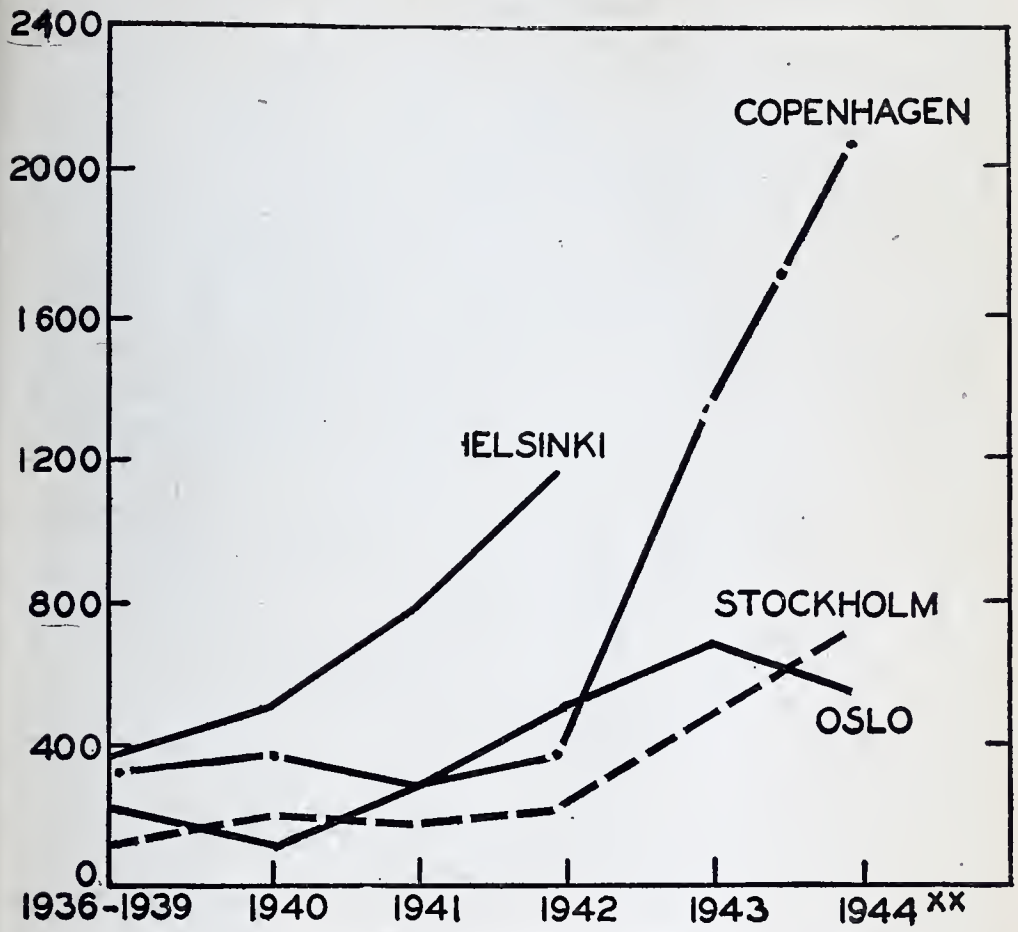
In the capital cities of the Scandinavian countries similar trends are found. This is illustrated in figure 3 where the reported number of cases of syphilis from 1936 to 1944 is given for the Scandinavian capitals of Copenhagen, Oslo, and Stockholm as well as for Helsinki.

FIGURE 2.—*Syphilis Increase in World War II, 1940–1944*



x) 1944: Norway—5 months
Sweden—6 months
Denmark—6 months

FIGURE 3.—*Syphilis Number of Cases Reported in Capitals of Finland, Sweden, Denmark and Norway, 1936–1944*



x) 1942: Helsinki—6 months xx): Copenhagen—6 months
Stockholm —6 months
Oslo —7 months

The incidence when computed per 100,000 inhabitants of these capitals is seen from table 3:

TABLE 3.—*Syphilis in northern European capitals during World War II*

Helsinki	380	(1942)
Oslo	210	(1943)
Copenhagen	170	(1943)
Stockholm	70	(1943)

Incidence per 100,000 inhabitants per year.

While Helsinki has relatively and absolutely the highest incidence of syphilis in the northern countries, Oslo, boasting the lowest absolute figure, has relatively more syphilis (per 100,000 population) than Copenhagen and Stockholm.

The parallelism of the records in all 3 Scandinavian countries seems to justify the previously prevailing supposition that the venereal disease administration is closely similar in each of the 3 Scandinavian countries. Secondly, it suggests that the prewar system of notification of venereal and other diseases has not been much interfered with during the occupation. It is further reasonable to assume that an evolution, at least similar to that in Scandinavia, has taken place in the rest of Europe during the war. This is confirmed by the fragmentary evidence from other European countries, previously referred to in this presentation. As a matter of fact, there is reason to believe that many parts of Europe probably have fared much worse than Scandinavia in this respect, particularly since the rising tide of syphilis in Scandinavia has not as yet reached prewar levels of many other European countries.

The Germans have, no doubt, made considerable efforts to control venereal diseases in Axis-dominated Europe. Occupied and other nations have presumably also made important efforts to check the increase. These efforts have evidently not been adequate, and it has been estimated that syphilis in Europe after the war might be found at tenfold its prewar incidence.

In the United States and Great Britain the increasing incidence of venereal disease following the outbreak of the war has, on the other hand, been checked by the machinery of the military and civilian health and welfare authorities, geared to bear upon these problems during wartime. In the United States the principles of attack have been formulated in the joint eight-point program of the United States Public Health Service, the United States Army and Navy in 1939. The passage of the May Act in 1941 cleared the way for a national policy against prostitution, and systematic efforts of case finding and case holding, early diagnosis, adequate treatment, posttreatment observation, prophylaxis, prevention and education have been cardinal factors in medical and allied professions' contribution to the physical fitness program of the United States at war.

Whatever the merits of the various efforts to achieve control of venereal diseases in Europe before World War II, their success (Scandinavia) or failure (Balkans) was only to a limited extent due to regional, inter-European, or international public health planning. On the other hand, the efforts of international cooperation and coordination in this field should not be underrated. Among these efforts were:

1. The important 1924 International Agreement of Brussels endeavoring to control the spread of venereal diseases by the maritime communications route.

2. The enquiry of 1924-1926 of the League of Nations' special body of experts in traffic in women and children, giving impetus to public opinion for government action against prostitution and the abolition of licensed brothels.

3. Commissions on venereal diseases, established by the League of Nations, instrumental in standardizing research in the venereal disease field.

4. The conventions and recommendations of the International Labor Office committing member governments to goals related to social security and medical care.

5. The International Sanitary Conventions with proposed revisions by United Nations Relief and Rehabilitation Administration (1944), and the Epidemiological Intelligence Service under the International Public Health Office in Paris.

6. The program of the health section of UNRRA, with whom may be resting, among other things, the control of communicable diseases among intruded and displaced persons during postwar repatriation in many parts of the world.

The Brussels agreement is the most specific antivenereal document, and has been signed, ratified, or adhered to by 57 countries. It calls, among other things, for the establishment and maintenance of services for antivenereal treatment of seamen and watermen in the principal ports of the world. The agreement was instrumental in bringing into the open, and recognizing the facts: (1) That venereal disease was an important "water-borne" disease, in a new sense of this word; (2) that seamen were easily exposed to venereal infections in the great ports, and perhaps liable to develop venereal disease to a greater extent than most other professions. This was a very important international advancement.

To what extent the Brussels agreement has served the functions for which it was designed still remains open. A general appraisal of the practical application of the articles and the results obtained has yet to be made. Such an appraisal would be most important as a preliminary to future necessary improvements of antivenereal treatment of seamen and, above all, for case holding, control, and follow-up of venereal disease among that professional group. The data gathered might form an important document in the reshaping of immigration laws in various countries, which in peacetime did not recognize the need for antivenereal treatment of foreign seamen beyond the stage of infectiousness.

The antivenereal treatment of merchant sailors is of vital concern to Scandinavian countries, perhaps particularly to Norway, where more than 1.2 percent of the entire population of the country before the war was engaged as seamen in overseas and home trade. The Norwegian merchant fleet was the third largest in the world, and many ships before the war fared the high seas for years at a time without calling at home ports. World War II and the German invasion of Norway brought this fact acutely to the attention of the Allies when the great Norwegian overseas fleet sought allied ports, making it subsequently possible to maintain allied lifelines of supply in the critical years of 1940-1941, before the United States entered the war.

The public health authorities of the Norwegian Government in London became conscious early in the war of its special obligations to the merchant seamen, at a time when disease rates in general and venereal rates in particular started their upward trend in allied and enemy countries. Legislation focused on health protection by means of a network of Norwegian overseas public health clinics in the larger ports of the United Kingdom, Canada, the United States, Iceland, and India, by a system of hospitals, convalescent and rest homes, as well as recreational facilities in the form of seamen's hotels, reading rooms, clubs, and similar means. In the clinics, emphasis was put on antivenereal treatment, and special preventive measures against venereal disease were introduced

aboard ships. Convenient and free access to rubber and sulfathiazole, educational efforts by pamphlets, films, and lectures formed part of this antivenereal program. Of special interest is considered to be the introduction of sulfathiazole for self-treatment aboard ships according to instructions by the Norwegian Public Health Service, if symptoms of gonorrhea developed at sea.

Alcohol is often a contributory factor and the indirect cause of promiscuous sexual practices resulting in venereal diseases. The Norwegian sailors have for almost 5 years during the war been cut off from family and social connections in Norway, and may therefore easily resort to alcohol as a suitable and practical anesthetic while ashore. With good results the tendency to excessive drinking has been counteracted by offering alcohol for restricted consumption in the Norwegian seamen's hotels, reading rooms, clubs, etc., in an effort to curtail the facilitation of exposure to venereal disease. It has by and large been possible to measure the effect of this program. While alarming reports of rising venereal disease rates among seamen in 1940 and 1941 had come from health authorities in England (Hutchison (*2*)) and U.S.A. (Burow (*3,4*)), statistics from the Norwegian Public Health Service clinics in Halifax and New York seem to indicate encouraging results from 1942 to 1944. About 7.6 percent (1,456) of a total of 19,000 sailors examined from 1942 to October 1944 at these clinics was recorded as needing antisyphilitic treatment. Studies of the venereal disease rates in this group for comparable 4-month periods in 1942, 1943, and 1944 (table 4) are encouraging and show considerable reduction in new cases of gonorrhea (48 percent) and particularly of syphilis (66 percent).

TABLE 4.—*Prevalence of venereal diseases in the Norwegian Merchant Marine 1942–1944 Norwegian Public Health Service Clinics in Halifax and New York*

	Rates per 1,000 seamen 4 months, period[1]			Reduction in percent
	1942	1943	1944	1942–44
NEW CASES				
Syphilis	17.3	10.5	6	66
Gonorrhea	11.7	7.1	6.1	48
Chancroid and lymphogranuloma venereum	2.9	2.9	2.2	----
Total	31.9	20.5	14.3	55
Number of seamen examined	5,717	6,152	6,314	----

[1] April through July.

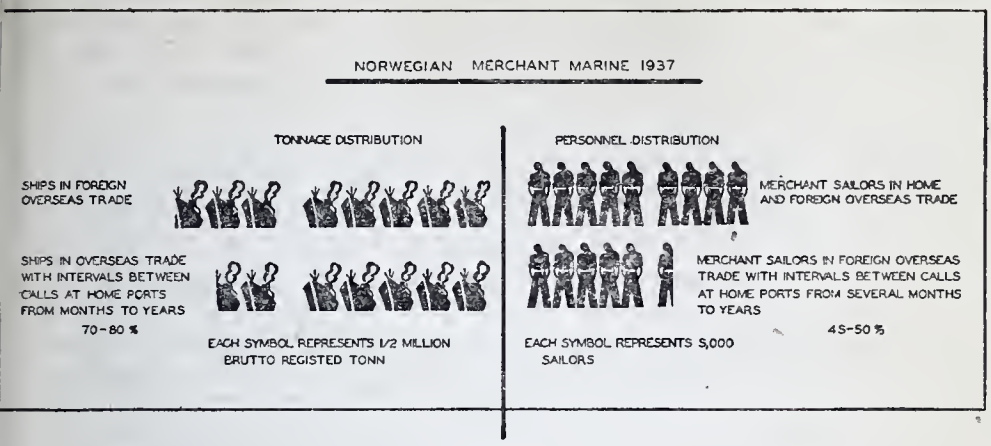


FIGURE 4

The venereal disease rate per 1,000 men per year, on the basis of these data would be 95.7 in 1942, 61.5 in 1943, and 42.9 in 1944, a total decrease for all venereal diseases of about 55 percent. The figure for 1944 corresponds roughly to the yearly incidence of venereal disease in the United States Army in 1932.

It is believed that continued systematic efforts with preventive programs, with rapid and intensive arsenotherapy, penicillin and other improved methods developed in the United States and the United Kingdom during the war may continue to show results.

The venereal disease problem of Norway is thus of a dual nature, namely one, largely among seamen, outside of Norway, exhibiting encouraging results; and one still unchecked, sprung up in Norway during the German occupation. It is hoped that continued close and friendly cooperation with the health authorities and experts of Allied nations will give us even stronger weapons again to tackle the job of reducing venereal disease in Scandinavia to prewar levels, and with improved methods obtain results within a relatively short period of time.

The experience gained by the United Kingdom and the United States and other maritime nations during World War II should form an important basis for the future check of the frequent spread of venereal diseases by the maritime route. A true international health-book system for seamen, possibly combined with passports, as well as reporting of syphilis among foreign seamen between nations to the respective public health services of the various countries may be suggestions to further this end. The Brussels agreement of 1924 should be revised and expanded to include new principles and advanced knowledge for handling venereal disease problems with due regard to the tremendous development in maritime and aerial communications.

It is clear that the postwar venereal problems in the region of Europe alone may be complex, but the difficulties to overcome may be even greater in other regions of the world, particularly where illiteracy and prostitution prevail. But however great the total task, one of the objects of the future international health body and its regional suborganizations must clearly be to reduce the venereal disease rate to the barest possible minimum. Medical

and allied professions as well as public opinion must no longer be satisfied to regard typhus, yellow fever, etc. as the principal international epidemiologic concerns. The time has come for an internationally planned and coordinated crusade against the most widespread of all communicable preventable maladies—the venereal diseases. Standardized medical and public health procedures, including serologic and venereal disease census methods, developed during the last years; social welfare and security measures; the practice of individual, clinical and organized medicine; informative and educational campaigns and programs for the profession and the public, as well as stimulation of research and suppression of prostitution, charlatanry and quackery, are but some of the weapons at our disposal. Public health problems all over the world are fundamentally the same. This probably contributed to make health work before this war one of the most successful of international undertakings. We might benefit immeasurably if the preparatory work and basic planning for the coming international health body could be undertaken before this war is over. An international health meeting called now to further this end would be of the greatest significance. The gap between the temporary functions of UNRRA and those of the future international security organization might thereby be reduced to a minimum.

Only by coordinated international planning and cooperation in the health field can we advance toward our goals: freedom from disease, and the establishment of a permanently valid international gold standard of health, to the benefit of large and small nations alike.

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The Chairman: I must take a moment to say that those of us who have seen the operations of the Norwegian Health Service during these years of war are filled with great admiration for what it has been doing. I can say in a word what I think Dr. Guthe was saying in other words, that the gallant Norwegian sailors have been so busy fighting the battles against the submarine on the North Atlantic supply lines that they have had no time in which to acquire venereal diseases.

Some of us who are old timers in this fight recall the great inspiration which came to us by a personal message, a series of lectures delivered before the American Public Health Association and other organizations in this country in 1935, by Dr. Einar Rietz, the Chief Medical Officer of Health of Stockholm. Within just the past few weeks I have had a personal letter from Dr. Rietz, introducing a colleague of his who is representing the Swedish Ministry of Health, Dr. Axel Hojer, who is also the Chief Medical Officer representing the Committee on Medical Research for the National Research Council of Sweden and now a technical adviser to the Swedish Legation. I should like to present to you, not for a speech but for a bow, Dr. Axel Hojer of Sweden.

The hearts of all Americans quickened, all of us were filled with joy when news came day by day of the liberation of France. I had the great pleasure on the evening when it was announced that Paris was liberated of dining with the distinguished representative of the medical profession in France, who has been in this country for some years, Dr. Andre Meyer, and one cannot imagine the joy in the heart of that great scientist at the news that Paris was free.

It was very late in connection with the preparation of this meeting that we learned of another distinguished French colleague who would be present. May I present to you Major Bertrand Gau of the French Military Commission in Washington. It is deeply regretted that, owing to the lateness of the hour, we shall have to forego the pleasure of listening to his address.

INTERNATIONAL CONTROL OF VENEREAL DISEASES IN THE POSTWAR PERIOD: WITH SPECIAL REFERENCE TO FRANCE

BERTRAND R. GAU, *Major, M. C.*,
French Army Medical Section, French Military Mission

It is probable that a postwar program for the control of venereal diseases in France has been already established but, so far, no information has been made available in this matter, communications between France and foreign countries still being very scant. However, the problem can be outlined, necessarily very scantily, as follows: Two aspects are presented: (1) The individuals detained in Germany, as prisoners of war, as compulsory workers, or those who were banished because of political beliefs and sent to concentration camps, should be checked for venereal disease before their repatriation. (2) Every French person who has remained in France should be examined as to his or her venereal disease status. For both categories, the results of examination should be recorded on a "Health Card," which card every one would be required to carry.

Checking the first group would mean the examination of a total of two and a half million people. A great difficulty in this will be because of the fact that every one of these persons will strive to return to his home at the earliest possible time following the armistice, and, therefore, the examinations will have to be performed without delay. That the prisoners of war are not all confined to camps, some of them being scattered in various compulsory activities, presents another great problem. Those prisoners who have been confined to camps and also the politically banished will surely be found to be in a very poor state of health. However, they should have a low rate of infection with venereal diseases due to their isolation. The prisoners who have not been in camps would have to be collected into groups before being examined.

Sanitary stations will have to be provided in order to take care of all those individuals who in their eagerness to return to their homes, had escaped the check-up and were endeavoring to cross into France. These stations will have to be established along the border, on railroads and highways.

The compulsory workers will have been living in rather free communities scattered in small groups all over Germany. Many of these workers are young people, isolated from family environment, and the forecast of their venereal disease infection will not be good. It can be estimated as from 8 to 10 per 1,000. This means that 10,000 to 15,000 patients will require adequate treatment before they can be released for repatriation. Nevertheless, it would be wise and safe to provide for a blood test for all these individuals before their departure from Germany in order to determine who should be treated.

A recommendation by this conference that blood tests be performed on all persons who are to be repatriated would strengthen this project. Such a recommendation would also aid the international organization in charge in obtaining materials needed to perform this tremendous laboratory job in the shortest time.

Would it be possible to plan for the laboratory equipment and personnel to perform 20,000 blood tests a day, the work to be done in small laboratory units scattered over Germany, in prison and workers' camps? Treatment must be provided for after examinations are made.

Since among the venereal diseases, syphilis is the major evil and requires the most of our attention, I will not discuss the treatment of the less common venereal diseases nor the treatment of gonorrhea, which seems to be efficiently taken care of by the sulfonamides and by penicillin.

Arsenical products and bismuth derivatives will have to be used for the treatment of syphilis for a long time in France owing to the complete lack of local production of penicillin. It is probable that the "rapid treatment" of early syphilis by arsenical products will be more widely utilized in France after the war, since it has been proved so effective in the United States.

It would be highly valuable if this national conference could have the various antisyphilitic drugs classified, recommending those which have been proof-tested and disregarding those which might be harmful or obsolete. At the same time a standardization of the treatment in every detail for large scale application and a preference list according to availability would encourage all nations to benefit from the very large experience acquired in the United States. If penicillin has proved its great efficiency, as well as its rapidity in curing primary syphilis, that fact should be recognized, and it should be recommended as the best therapy.

The international organization of the United Nations Relief and Rehabilitation Administration, known as UNRRA, is chiefly concerned with the transportation of all "displaced persons" and it will have to handle this migration as soon as the military command requests it. It will be a tremendous undertaking, involving at least 30 million human beings all over the world. We know that plans for transportation have been already drawn up, together with provisions for prevention of communicable diseases. We insist upon the necessity of including venereal diseases within the so-called communicable diseases.

French statistics show that the dissemination of venereal disease has greatly increased when large groups of people are moved. During 1941 and 1942 the number of new cases was twice what it was in 1939; in 1919 the rate of venereal diseases in the French Army attained 20 per 1,000, which is enormous when compared with the average rate in peacetime of 2 per 1,000. It would, therefore, be of great value if this conference would strongly recommend the checking for venereal diseases and the treatment of the venereally diseased patients prior to their repatriation.

Penicillin has been distributed in small quantities for civilian use and will continue to be so distributed for the duration. But as soon as the fighting is over it is to be supposed that surplus stocks can be made immediately available. Your recommendation that

this surplus stock be turned over to the Health Division of the UNRRA would give that organization a potential help in performing its activities. This same recommendation could be applied to the surplus sulfonamides to be used in the treatment of gonorrhea.

Carrying out such an extensive problem as this repatriation of the French will be linked with political conditions inside Germany immediately after the armistice. It is hoped that our Allies will lend all facilities by means of an International Commission of Health Control.

The problem of postwar venereal disease control inside France will have to be undertaken on a large scale in order to reduce the weakening factors within a population which has already suffered from long starvation.

Two laws have already been issued by the French Government in order to establish compulsory treatment and follow-up of venereal disease patients: A law of Nov. 29, 1939, directing the compulsory treatment of every venereal disease patient, and a law of Dec. 31, 1942, providing for the compulsory declaration of all venereal disease patients and giving them all facilities for free treatment and follow-up. This legislation provides effective weapons in a campaign for the identification and care of venereal disease patients.

For many years prophylactic organizations worked actively in every important French town, in the "Anti-Venereal Dispensaries." The French population was 42 million; in principle there was a dispensary for every 80,000 inhabitants, or approximately 500 for the entire country, 20 being located in Paris. Their purpose was to take care, free of charge, of every consulting patient, but there was no legislation to enforce the use of such facilities. Since the new legislation provides for compulsory declaration and treatment, patients will have to report periodically after discharge.

It is expected that in the very near future a large majority of the French adult male population will have come under medical control and classification. They would have been from the following categories: Prisoners of war and politically banished, compulsory workers in Germany, refugees in France, military men before their discharge, and government employees and industrial workers. Within a few years every school boy will probably be submitted to a careful medical examination at the time of his enrollment in school and also to periodical check-ups throughout his school days.

It is certain that part of the antivenereal disease program will be the education of the people by various means, such as, educational conferences in high schools and military barracks, educational films, radio speeches, and posters in public places. These various educational means will warn the people of the evils of venereal diseases and will encourage them to report immediately after a possible contamination.

The individual health card, that will be issued to every person examined, will be the first major step toward a general program of health survey that will apply all over France. This card will help in the control of venereal diseases, as well as such prevalent diseases as tuberculosis and cancer. In addition to providing each individual with a health card, the health service will keep records of all cases and assume the responsibility of following them up and

treating them as long as necessary. These measures will constitute a major advance in the effective control of venereal diseases by making it impossible for such a patient to disappear as soon as he becomes symptom free.

The realization of this program will involve much work and the expenditure of large sums of money, but the French Government is determined to assume this burden as an essential part of the moral and physical rehabilitation of the French people. Confirming this opinion, the French Minister for Public Health, M. Francois Billoux, stated in a cablegram received at New York on Oct. 28, 1944:

"The Health Ministry will be the relief organization for the sick and wounded and I intend to make it a Ministry for the prevention of diseases. It will cost billions, but it will keep the French population in good health and maintain productive workers. We must draw up the balance sheet of the health situation and a campaign of disease prevention must be undertaken on a large scale. The health of the French population is deficient because of the war. It demands heroic measures. We shall increase the use of all health precautions, sanatoria, disease prevention centers, antivenereal dispensaries, hospitals, and rest centers for underprivileged children. I am thinking of the children in France today and of the babies of tomorrow. France must build up her birth rate."

FRIDAY MORNING SESSION

November 10, 1944

The meeting convened at 10 o'clock. Dr. J. R. Heller, Jr., presided.

The Chairman: We continue the conference with a general session devoted to topics of general interest selected for their appropriateness for the conference, and for their timeliness insofar as postwar plans are concerned. The first address will be by Medical Director Udo J. Wile of the University of Michigan.

RAPID TREATMENT FOR SYPHILIS

UDO J. WILE, M.D., *Medical Director (R)*,
United States Public Health Service
Professor of Dermatology and Syphilology, University of Michigan

The various rapid treatment methods now in use for the treatment of syphilis represent an experimental effort to shorten the course of a disease which in the past required many years to effect protection against its serious late sequelae. The concept that the progress of syphilis could be aborted and that cure in the clinical sense could be achieved is, however, not entirely new.

Medical history furnishes several attempts to introduce treatment procedures which were short cuts to the accepted methods of the particular era in which they were introduced. From the very beginning of specific therapy, enormous doses of mercury were introduced, so large indeed that they produced the well known effects of mercury poisoning, while at the same time healing the lesions. The excision and cauterization or destruction of the primary lesion, for many years, was believed to be of distinct advantage and a short cut to cure by eliminating the original focus of distribution of the infection. With the introduction of salvarsan, Ehrlich believed that he had achieved a method of eliminating in one dose the newly discovered infective agent. How far this hope, as well as the previous attempted methods, fell short of their desired results was all too obvious in a brief period of time. In 1909 and 1910 the first successful attempts to achieve both early serologic and clinical cure were secured by the late Sigmund Pollitzer who combined old salvarsan given in rapidly repeated large doses over a short period of time, with full doses of injections of insoluble mercury salts. Pollitzer's important contribution to rapid therapy, published in 1916, attended by a large measure of success, has been quite overlooked in all of the recent publications on rapid treatment methods. It would seem not out of place to quote a paragraph or two of this farsighted observer's contribution to rapid therapy.

"* * * Salvarsan should be administered in sufficient doses, repeated at such intervals that the blood is kept charged with the drug for several days, continuously. The elimination of salvarsan from the system takes place very rapidly. It begins almost immediately after an intravenous injection; the drug may be detected in the urine within an hour or less, and at the end of twenty-four hours probably nine-tenths of the amount injected has been excreted. The full effect of salvarsan is exerted therefore only for a very brief period, a few hours at most; and any organisms in the

system that are not killed within this short time, necessarily will survive the small proportion of salvarsan retained during the succeeding hours or days. If, therefore, we wish to maintain an adequate concentration of salvarsan in the blood for a longer period, the injection of the drug must be repeated at intervals which should be measured by hours rather than by days or weeks. The theoretical consideration here advanced requires that injections of salvarsan should be made at least three times in twenty-four hours.

"* * * There is, however, no great difficulty in making our salvarsan injections daily, and this is the plan I have of late employed, giving three full doses of salvarsan on three successive days. By this method cases that have in the past remained Wassermann-positive in spite of repeated courses of salvarsan and mercury at weekly intervals, have responded with a negative result."

To those interested in modern intensive therapeutic procedures, a review of this interesting communication by Pollitzer is most refreshing and informative.

Since the second decade of this century, no further significant efforts leading toward rapid treatment appeared until the work of Hyman, Chargin, and Leifer, who introduced the intravenous drip method of the arsenicals given in large doses over a short period of time. By thus achieving a high concentration of arsenic in the blood stream, they successfully demonstrated the possibility of eradicating the disease in its early stages. This valuable study was not intended to be distributed to the general medical public as an outpatient or office procedure. It may, however, be said to be the forerunner of the methods now used with a considerable degree of success during the present emergency.

The present era of rapid treatment methods represents one of the therapeutic advances actuated and stimulated by the necessities and exigencies of the war program. The importance of venereal disease control becomes much more important in time of war. The reasons for this are, of course, obvious. The large concentration of young people drafted into military and industrial activities demands accentuated efforts to control the increased venereal disease rate which inevitably follows such critical movements.

It became, therefore, the duty of those concerned with the health of the Nation, to devise means of maintaining, if possible, the peacetime level of venereal disease rate in the face of a greater degree of exposure and a threatened increase of venereal diseases. To this end, the United States Public Health Service, Venereal Disease Control Officers of the Army and Navy, and the Venereal Disease Subcommittee of the National Research Council have joined in a cooperative effort to devise means of rapid treatment of syphilis which could be applicable to those in the armed services, to such persons as could be quarantined by State or Federal statutes, as well as to patients who might seek treatment voluntarily. These joint efforts, if successful, could in time then be turned over for general use to the medical profession, when sufficient time had elapsed to prove their ultimate effectiveness and to establish relatively safe procedures for ambulatory practice.

In a general way the preliminary treatment procedures were all modifications of existing methods in that they embodied giving

larger doses of arsenic and heavy metal over a much shorter space of time.

These various methods, initially used and to a large extent still in use with constant modifications, are listed as follows:

(1) The administration of arsenical drugs by continuous intravenous drip extended for 5 days, and more recently over an 8-day period.

(2) The administration of multiple syringe injections over periods varying from 4 to 8 weeks.

(3) A concentration of previously utilized intravenous injections from the old accepted one-a-week method, to daily injections over a period of 10 days, 25 days, and in some instances 30 days.

(4) Treatment with arsenoxide in a single dose, together with fever induced in a hypotherm.

(5) The use of multiple syringe injections of arsenoxide over a period of 10 days with 4 bouts of fever induced by intravenous injections of typhoid vaccine.

With the exception of the 1-day fever plan, the other condensed methods of treatment were all supplemented by more or less weekly injections of insoluble bismuth preparations. Until very recently these methods, with certain minor modifications, constituted the newer rapid treatment procedures in use in that portion of the lay population which could be reached through public health and military epidemiologic sources, and the plan of concentrated multiple syringe injections plus bismuth over a period from 8 to 12 weeks was in general use in the armed services for patients with recently acquired syphilitic infections.

The entire program within the last year has been greatly extended and modified by the introduction of penicillin alone, and in combination on the one hand with bismuth and arsenoxide and on the other with fever bouts induced both by typhoid injections and by the hypotherm.

During the past two years, 63 rapid treatment centers, established throughout various States, financed through Federal Government agencies, maintained by the several States, and medically conducted by the United States Public Health Service, have treated over 25,000 cases of early syphilitic infection by one of these methods. In addition to this, a far greater number of soldiers and sailors have been subjected for their early infections to one or another of the multiple syringe programs combined with bismuth.

Added to these there are several hundred cases, or possibly a greater number, which have been treated successfully by physicians outside of the United States Public Health Service and the armed forces. A beginning of rapid treatment, at least, has thus been introduced into general medical practice. It is unfortunate that at this time the number and the results of patients so treated cannot be determined.

The evaluation of these treatment systems can, at this time, only be appraised with regard to the immediate therapeutic effects. The results of rapid treatment procedure upon the possible late sequelae of syphilis and also the deleterious toxic effects which the patients may have sustained can be determined only after many years have elapsed. It seems quite evident, however, from the most careful observation and follow-up, that the infections would seem

to have been arrested, aborted, and, according to serologic studies, serologically reversed in a very large percentage of cases.

The many cases of actual reinfection which have taken place in patients treated by rapid treatment methods not only indicate that their infections have definitely been aborted, but they suggest a reconsideration of the existing criteria for reinfection.

In addition to the 25,000 cases which have been treated in the State and Federal rapid treatment centers during the past two years, 836 reported cases of acute infectious syphilis have been treated with penicillin either alone or in combination with arsenoxide, and arsenoxide and bismuth. A smaller number have, since this time, been treated by combinations of penicillin with induced fever. Of the 836 reported up to and through July 15, 296 have been treated with 2,400,000 units of penicillin, 48 cases have been treated with 1,200,000 units, 458 with 600,000 units, 107 with 300,000 units plus 320 milligrams of arsenoxide, and finally, 27 with miscellaneous numbers of units. A much larger number than this have been treated, but reports from them are not yet tabulated and available as of this writing.

With these various methods at hand and with an experience of but two years in connection with the various treatment schedules employing arsenoxide and bismuth, and only a few months of observation of rapid treatment methods using variations of penicillin treatment, it is obvious that nothing more than a preliminary appraisal of therapeutic results can be determined at this time.

It may be stated in general that all of the methods employed have given apparently satisfactory therapeutic results as determined by the rapidity of dissolution of lesions, of the approach to seronegativity in those patients who were positive, the maintenance of negativity in those who never became positive, and in the general low relapse rate.

In determining presumptive success or ineffectiveness of the treatment, it seems wise to regard those cases as treatment failures in which the patients failed to achieve seronegativity if positive, those who achieved seronegativity and then had a serologic relapse, and lastly, the obvious cases of those which relapsed clinically. With these criteria, comparable results were achieved with all of the treatment methods prior to the use of penicillin. The largest number of relapses, generally speaking, occurred with the methods employing the smallest doses of arsenoxide. The figures derived from the various methods employed, while demonstrating minor differences, tended to show that about 80 percent of patients subjected to rapid treatment could be regarded as probably successfully treated, with the remaining 20 percent regarded as failures based on the criteria above mentioned.

I am quite convinced that by including as failures such patients who never achieved seronegativity but who nevertheless remained clinically well, there were many undoubtedly rendered noninfectious by their treatment. To this extent, these could be included in those contributing to the primary aim of the treatment program, namely, to sterilize the infectious carrier. In this group of patients there were many who carried a persistently low titer and some of these, at least, eventually could ultimately be expected to become seronegative.

These figures must also be tempered to a small degree by the bona fide cases of reinfection in which the treatment program succeeded in destroying the original infection, and the patient being reexposed became again seropositive and thus is included in the treatment failures.

I do not believe that these figures are better than those that could be achieved by the treatment of infectious syphilitic patients with conventional methods of treatment extending over a period of 2 years or more, where such treatment could be completed. In fact, my own experience with conventional treatment has been attended by a higher percentage of success.

It must be recognized, however, that the type of individual sent to the rapid treatment centers represents a far different social and economic group than could be cared for over a long period of time in a private clientele. The many thousands of patients subjected to rapid treatment methods in our rapid treatment centers were those who, under ordinary circumstances, would get either no treatment at all or would attend an outpatient dispensary for a few weeks at the most, or to such time as all of their symptoms had disappeared. As carried out in the ordinary dispensary practice, it has been estimated that not more than about 30 percent of the patients in this large group receive sufficient treatment to protect them from infectious relapses.

It would seem desirable at this time to discuss briefly the various advantages of all of the rapid treatment methods as carried out in the program of venereal disease control and to point out their very obvious disadvantages.

The advantages of the rapid treatment methods can be briefly summarized as follows: All of the treatment necessary to give practical assurance of noninfectiousness of the individual can be carried out in a remarkably short period of a few days or a few weeks. The difficulty of case holding under these conditions is, therefore, answered for this type of patient.

The next factor of great importance is the fact that during the period of infectiousness, the patients are hospitalized, out of circulation, and thus not contributing to the spread of their disease. The degree to which this particular factor has kept down the incidence of syphilis is unfortunately not determinable. It must, however, be obvious that the spread of infection from this sexually promiscuous group has been greatly cut down by their isolation in hospitals over the treatment period.

A third point, as yet of undeterminable importance not only to the physical but also to the economic status of the patients, is the likelihood that many of them have been saved the late sequelae of inadequate or untreated infections. Time will determine for us more definitely the significance of this possibility, but the present high figures of apparent successful disease arrest and cure, justify an optimistic outlook so far as late sequelae are concerned.

Next in importance is the publicity given to the rapid treatment schedules as it reflects itself upon the program of venereal disease control among the lay population. The educational phase of venereal disease control is greatly enhanced by any proper publication relating to methods of prevention and treatment. Mention, however, must be made of the unfortunate publicity given to rapid

treatment methods in certain lay journals and magazines. Assurance was given that syphilis could be cured in a day, without emphasizing that this method was still in an experimental stage, that it did not apply to syphilis as a whole but only to the very earliest infections, and that the results had not been followed sufficiently long to give assurance of ultimate success. Premature publications of this type are a handicap rather than a help to the program.

Turning now to the disadvantages of rapid treatment, we must cite first the loss of time incident to hospitalization. This entails an economic loss, not only to the patient but to the employer as well. A second obvious disadvantage is that in any program as large as the one under discussion carried out in the time of national emergency, we are dealing essentially with a mass treatment. Under conditions of mass treatment procedures, we endorse the treatment of the disease rather than that of the patient. There is perhaps no other disease in human pathology in which a greater degree of individualization and appraisal is indicated than in syphilis. Many considerations other than the disease itself should normally enter into the method of procedure: age, duration of infection, the history of previous treatment, the type of syphilide present, the social and economic status of the individual, and last, but not least, the presence of concurrent or intercurrent disease. These are all factors which indicate individualization of procedure, which is naturally not possible, except to a limited degree, where large numbers of patients are treated, and where, as in the case of our rapid treatment centers, frequently staff and equipment are far from ideal.

The most important disadvantage of rapid treatment is the anticipated greater risk to the patient. In all of our treatment schedules, in which we have shortened the period and increased the dosage of arsenoxide and heavy metal, we have increased the risk to the patient's health and notably increased the mortality rate following treatment.

I think it may properly be stated that no treatment of any disease can be ideal or nearly so, in which the drug, substance, or biologic used is so toxic that it can seriously injure the patient while curing his disease and, in some instances, lead to death. This has been the case with the syphilis treatment program as carried out ever since heavy metal and arsenic have been introduced into syphilis therapy. Many cases have died as a result of treatment along conventional lines. Those who have had hospital experience of many years can attest to the fact that patients have all too frequently died as a result of mercurial nephritis or of bismuth intoxication, and since the introduction of arsenic, a far larger number have succumbed to exfoliative dermatitis, agranulocytosis, severe liver damage, aplastic anemia, and hemorrhagic encephalitis.

Attention to the mortality of syphilis treatment has never been emphasized in past years because no extensive study, such as is being carried out today, has been made. The deaths and near deaths from syphilis therapy will undoubtedly increase when the treatment program is pushed into a shorter period and when larger doses of the drugs in use are employed. That no form of rapid treatment employing arsenic and bismuth can be considered as safe as when the same drug is used in conventional forms of treat-

ment is indicated by the fact that we have encountered hemorrhagic encephalopathy, agranulocytosis, severe ninth-day erythemas, exfoliative dermatitis, and jaundice in all of the treatment methods used. As stated, however, these complications are not new in syphilotherapy, but the rapid methods have increased their frequency.

I am satisfied that many of these unfortunate occurrences were unpreventable accidents and that for the most part they occurred in arsenic susceptible individuals in whom it was impossible to predicate in advance their intolerance. I may state that our mortality rate has been decreased by three factors: by added experience of our officers, for many of whom the treatment program was quite new; by modifications of time and dosage, and by remedial methods and cessation of treatment when intolerance is first manifested. The incalculable benefits to the large number of patients successfully treated outweigh, in my opinion, all of the disadvantages just cited.

For centuries the treatment program of syphilis has been in a decided state of flux; at no time has this been more striking and evident than at present. The introduction of penicillin into the syphilis treatment program may reasonably be expected to lead to a marked reduction in the risk factor of treatment. As you have already heard, the use of this substance alone has been attended by a considerable degree of success when viewed from the immediate clinical response and serologic reactions over a short period of time, and at the same time with few toxic reactions. When used together with bismuth and arsenoxide, however, we again encounter toxic results in a few instances.

It may properly be anticipated that penicillin, and other like substances to be developed in the immediate future, will provide us with a means of treating syphilis in which we have a high index of therapeutic activity and a far lower toxic response than must be anticipated with the intensive use of arsenic and heavy metals, either alone or in combination with penicillin.

It does not seem desirable at this time to recommend the treatment programs now employed in rapid treatment centers and in the armed forces for use in general medical practice. The various methods now in use should still be regarded as experimental expedients of wartime medicine. It is safe to predict, however, that the results so far achieved will ultimately lead to safer methods with a far less expenditure of time and money than is required when treatment is carried out on conventional lines.

The Chairman: It is desirable to have but one discussion of these morning papers since the general discussion will be carried out in the section meetings. Dr. Carl V. Reynolds of North Carolina, who was to have discussed Dr. Wile's paper, is unable to be present. I wonder if the State Health Officer of South Carolina, Dr. Benjamin F. Wyman, would like to discuss rapid treatment.

Dr. Benjamin F. Wyman: Thank you, Dr. Heller, but I do not think I can add anything to this subject which would be of interest to this crowd.

The Chairman: The next speaker is Dr. J. F. Bredeck, City Health Officer of St. Louis.

EPIDEMIOLOGY OF THE VENEREAL DISEASES

J. F. Bredeck, M.D., *City Health Officer,*
St. Louis, Mo.

Every week the United States Public Health Service journal **Public Health Reports** is received on the desk of every health officer. In the chapter, "Prevalence of Disease," we have the text for my remarks, "No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring." Here we have in one sentence the crux of our problem of epidemiology in the control of the venereal diseases. It is not necessary for me to point out to this audience that venereal disease control is a major public health problem. I am not certain that we fully realize all of the implications nor do I feel certain that we know its real size. It is a public health problem because any such problem becomes one of public concern when, because of its nature and extent, its solution requires organized group action.

In this community we have more venereal diseases reported than all of the other infectious diseases combined. The problem is an old one. It is of interest to note that in 1864 according to the minutes of the Board of Health the infectious diseases admitted most frequently to City Hospital were the venereal diseases, syphilis—170 cases, gonorrhea—13. This was before we had the present perfected laboratory methods, so that the diagnoses were made on clinical findings alone. Incidentally, we had no automobiles, no radio, no movies, but we did have "the surrey with the fringe on top." In 1943 there was reported a total of 3,370 cases of venereal diseases, including 2,723 cases of syphilis and 574 cases gonorrhea. In 1941, 1,893 cases of venereal diseases were reported. So far this year there have been over 5,000 cases; the more we look, the more we find. It is obvious to anyone who has studied the problem that the venereal diseases have been on the increase for many years. And we have had this increase despite our wonderful discoveries in diagnosis and treatment. Wars have arisen during the years, always with similar conditions of increased interest in venereal diseases, always followed by prolonged periods of lethargy. The air is again full of talk about vice, juvenile delinquency, prostitution and Victory Girls—the same old story with every war for centuries. The "Whores de Combat" are ever present, but the uniform brings local conditions into bold relief. Medical officers in the armed forces are alarmed about conditions; if they only had been alarmed in civilian life, and if they only remain interested when they return to civilian practice after the war.

The Civil War, the Spanish-American War, World War I, and the present conflict have all brought venereal diseases to the forefront. Yet in the lethargic years between wars the same infections have been increasing year after year. The venereal diseases have always been contracted from the civilian population by the armed forces. The armed forces have not always appreciated what valuable service they might render by careful investigations of the sources of infection. Their rate of infection is directly related to the degree of infection in their local area. With each war, the mili-

tary forces have been in a position to give additional information as to the nature, extent, and sources of infection of these diseases to local health officers. We still, however, have very incomplete information concerning the incidence of venereal diseases in our civilian population. The last world war was responsible for the creation of the Venereal Disease Service in the Health Division of the city of St. Louis. Fortunately, prior to the present war increased interest was aroused and a complete reorganization of control measures was instituted. While the reporting of venereal diseases has increased remarkably in the past 6 or 7 years, it still is not satisfactory. The proportion of syphilis to gonorrhea reported in civilian population is at marked variance with the reporting of these diseases in the military services. The reporting of gonorrhea in civilian life today is just as incomplete as it was 80 years ago. For the past 30 years and longer we have had many epoch-making discoveries in diagnosis and treatment. Every decade has seen marvelous improvements in the methods for diagnosis and treatment; increased facilities for their use have been made available everywhere. Yet we continue to see the widespread prevalence of these diseases because we have failed in contact examinations.

Many meetings, local, State, national and international, have been held throughout the years and the greatest interest seems to be along diagnosis and treatment. We have placed too little emphasis and interest in epidemiology and the methods of case finding and case holding. These are tedious, time-consuming, costly, unattractive, and boring to so many, yet they are fundamental. If we wish to have the greatest application of our methods of diagnosis and treatment and their effect upon prevention of further spread of the disease, we must know when and where these diseases occur, and prompt reporting of cases as well as contacts is the first step after the diagnosis is made. The diagnosis cannot be made unless there is widespread education of the public to the effect that they must go to a physician for examination when they have suspicious symptoms or have been exposed to possible venereal infections. Patients, more particularly those who have exposed themselves, too often do not report promptly or at all to a physician. Unless they report promptly we cannot take action promptly, diagnose early, treat early and instruct early to prevent possible spread of infection. The physician must appreciate the necessity of reporting the cases and the contacts promptly. Failure to report cases, and more particularly the contacts, denies us the full use of preventive measures, examinations, diagnosis, treatment, and instructions.

In making out the morbidity reports, it is necessary to know when and where the infections were contracted, and under what circumstances, in order that the health officer may have information as to whether or not the conditions warrant special action by law enforcement agencies against organized prostitution. We all know that there are State laws and local ordinances which must be enforced in order to limit the number of exposures to organized as well as clandestine cesspools of infection. It is the function and duty of these law enforcement agencies to assist the health officer in breaking up these rendezvous. They must know the reasons

behind such laws and their importance in the control of the venereal diseases. The medical profession, law enforcement agencies, and the public as a whole must be thoroughly familiar with the facts concerning the dangers and the spread of these diseases.

In looking over morbidity reports for a period of years one is struck by the fact that the most neglected part of the reporting is the failure to mention possible sources of infection or contacts of the patients. We have failed largely in our control of venereal disease because we have only treated patients who reported to physicians for treatment. We have missed the most valuable opportunity for prevention of further spread of infections when we do not get the contacts or possible sources of the infection. Here lies the great field for endeavor for the future. Every physician seeing a case of venereal disease must spend time and patience in getting possible sources of infection. In this way only can we extend the benefits of treatment to rendering patients at least relatively noninfectious. We are treating only a small proportion of those who should be treated so long as we do not examine these contacts, treating those already infected, and making further examinations of those who are still in the incubation period. We are going to continue to fail in the control of these diseases if we continue to follow the cases instead of advancing ahead of them. We hear much about venereal disease control, when in reality we are hearing only about treatment control. There can be no adequate control without contact examinations.

We should have learned long ago from the control measures in tuberculosis a lesson of real value to us in the control of venereal diseases. In the control of tuberculosis, for over 40 years we have emphasized the necessity of contact examinations. We have never had any drugs to render the individuals noninfectious. The fatality rate of tuberculosis is the same today as it was 30 years ago; yet we have only one-third the number of deaths. This was all accomplished without specific drugs to render the individuals noninfectious. Diagnosis of cases and isolation and examination of contacts have brought about these remarkable results in tuberculosis control.

We should all know the conditions and circumstances under which venereal diseases occur. Illegitimate sexual intercourse, organized or unorganized, is the main cause of our problem. Law enforcement agencies certainly have a problem in dealing effectively with organized vice. Facilities for holding cases for sufficient periods of time to insure adequate treatment are essential. The case-holding programs have been inadequate in the past and are so at present because sufficient follow-up personnel has not been provided. Treatment and diagnostic facilities, even though still somewhat limited, are as a whole more adequate than any part of the program. We must of necessity continue to have too limited use of our diagnostic and treatment facilities because there is too little or no epidemiology to feed these services. Without epidemiology we do not put diagnosis and treatment to their greatest use.

There are certain fundamental problems involved in the control of venereal diseases that differ from those of the other infections. Legislation alone has its limitations. Law enforcement agencies,

schools, social welfare and church organizations, and health departments have their limitations; even the home has its.

The fundamental problem lies in man himself—homo sapiens. We have all been taught man's classification zoologically, but I wonder whether we understand the "sapiens" portion as we should. A better understanding of man himself would give us a better appreciation of the limitations that we work under in the control of the venereal diseases. Man has an intellect and a free will; he can think, reason, deliberate, decide, choose, and will. Take away his intellect and free will and he is no longer man. And with that free will he can decide to do right or wrong. He can decide only on the good or the bad and he is free in that decision. Since he has an intellect and since he has a free will he has need for moral law to guide him. You may call it what you will—moral law, the right code of ethics, reason, or the Ten Commandments. They are the fundamental laws to guide his actions. We accept or reject fundamental laws individually. Some we accept because we are guided by reason to believe they are right, and others because of the fear of being caught and punished for violating them. Other moral laws or codes of ethics are not accepted individually because the individual feels the consequences of the violations are not always too bad; the greatest of these is sexual immorality.

Illegitimate sexual intercourse, which is a violation of fundamental moral law, is the foundation of our venereal disease problem. I am not one of those who believe that human nature is any different today than it has been. Man is fundamentally the same. However, with certain infections being transmitted chiefly through illegitimate intercourse we, as health officers, must do everything we can to examine all individuals who practice it, and their contacts. And we have a further obligation in doing something about the major number of sexually promiscuous individuals who show no infection when they are examined. These cases are potential venereal disease cases. We examine them, discharge them, and do nothing more. Eventually they return with one or more of the venereal disease infections. If there is a group of individuals that certainly need all the resources of the community, it is that group of sexually promiscuous individuals. We have failed with them simply because we have not set up the proper machinery whereby the local health departments will direct these individuals to the welfare agencies in the community. The welfare agencies have not developed their resources as they should because we, as health officers, have not directed these individuals to them. Venereal diseases are truly a social problem and must be handled by society as a whole.

We hear a great deal about public health education but we have not developed that field to its fullest extent. A fuller understanding of man himself might better direct our programs of education of the future. Knowledge of the venereal diseases and their methods of spread is very valuable information which all should possess. However, an effort must be made to emphasize and direct the education of individuals along the lines of certain fundamental laws. As Ben Franklin says: "You can't sleep with dogs without getting fleas," so persons cannot expose themselves to promiscuous sexual intercourse without contracting venereal disease. Education is a slow process and one which continues with each generation, but

the fundamental nature of man remains the same. Unless he can guide his instincts with reason and intelligence and his free will by discipline, he will not avoid illegitimate intercourse. Whether he avoids illegitimate intercourse because of his knowledge of fundamental moral law or because of his fear of venereal disease, the results will be the same—a reduction in these infections. Theologians tell us that many individuals probably will get to heaven because of the fear of the devil rather than the love of the Lord. Knowledge and fear of venereal diseases should be sufficient reason to avoid promiscuous sexual intercourse. A fundamental principle of law appreciated by many is that the will to be governed is the most important factor in law observance. We can attack the problem by law enforcement agencies where there is organized vice, but law enforcement agencies and health departments alone cannot control the individual acts of men. Here we must call in all of the force of the community, social welfare agencies, and the schools and churches to unite in attacking the problem as a whole and not leave the entire problem to health departments and law enforcement agencies. In influencing the education in the home, the school, and the community, the fundamental moral laws are essential. It is well and good to teach the child arithmetic so that he can count his money, but it is equally important that he be taught the ethics on how he may acquire that money. Let us have more teaching of ethics and the true meaning of sexual immorality and the dangers of venereal diseases.

I emphasize these points here because we must radically change our attitude in our control program. We cannot continue to ignore the sexually promiscuous by only examining them and turning them out. They should be studied by health department services with qualified personnel and properly directed, when necessary, to the social and welfare agencies in the community. We are neglecting one of the most fertile fields for prevention. Contacts are the potential cases of the future and so are the sexually promiscuous. We can do a valuable piece of research and education here if we are fully realistic and understanding, and cooperate to the fullest with community resources. We know these individuals eventually contract venereal diseases and yet we do nothing about them. They have no disease, and we say "good-bye." Then when they are infected we move the elements to have them report regularly for treatments. Because we cannot do the whole job ourselves we do not utilize the community services already established for these very problems. It is a big job, but so is the control of venereal diseases. We are too impatient; we expect quick results. Everything is speed. We have just scratched the surface of the problem. Education is a slow process and the problems of education are not altogether new. If you want good epidemiology you must have patience. And speaking of education, Ralph Waldo Emerson had this to say about 80 years ago, and I quote: "Leave this military hurry and adopt the pace of nature. Her secret is patience. Do you know how the naturalist learns all the secrets of the forest, of plants, of birds, of beasts, of reptiles, of fishes, of the rivers and the sea? When he goes into the woods the birds fly before him and he finds none; when he goes to the river bank the fish and the reptile swim away and leave him alone. His secret

is patience; he sits down, and sits still; he is a statue; he is a log. These creatures have no value for their time, and he must put as low a rate on his. By dint of obstinate sitting still, reptile, fish, bird and beast, which all wish to return to their haunts, begin to return. He sits still; if they approach, he remains passive as the stone he sits upon. They lose their fear. They have curiosity too about him. By and by the curiosity masters the fear, and they come swimming, creeping and flying toward him; and he is still immovable, they not only resume their haunts and their ordinary labors and manners, show themselves to him in their work-day trim, but also volunteer some degree of advances towards fellowship and good understanding with a biped who behaves so civilly and well." In these lines we have the secret of obtaining good epidemiology in venereal diseases—patience and understanding, the technics and procedure of interviews.

We hear a great deal of discussion about reasons for the venereal diseases—poverty, housing, and a host of other specific causes. Of course, circumstances and environment play a role in all social problems, not excluding the venereal diseases. Aristotle made the statement over 2,000 years ago that the healthiness of a community depends on the quarters to which you expose them. But to look to physical environment alone and neglect the intellect and will of man is to overlook the two most essential factors in the control of venereal disease. Only to treat those infected, without attempting to guide those who are promiscuous by using all of the community's resources, is to have these individuals at some future time report with a venereal disease. Our education must be directed along lines that will encourage the disciplining of the free will and increasing the knowledge of the dangers of sexual promiscuity. To neglect promiscuous individuals and pay attention only to those who are infected is to miss a major part of the problem. We cannot wait for patients to present themselves when they have venereal disease, but must go further in examining and directing those who have been possible sources of infection. The knowledge of venereal disease alone without proper education along ethical lines and self-discipline will fail. Even Solomon with all of his wisdom, and with all of his wives and concubines, was not immune to choosing and willing to do the wrong thing.

I have attempted in this brief narrative to point out a few of the problems that I have observed over the years as fundamental to everyone in official positions to deal with venereal diseases. Venereal diseases will continue to be of major concern for many years to come, but we can curtail their ravages if we will think of these fundamentals. We will avoid expecting results too quickly. We will rededicate ourselves to the development of those services so necessary in the control of all the infectious diseases, and we will learn that we must thoroughly understand man and his environment. I will close with the sentence which should be pondered over and over again by every health officer: "No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring." That is epidemiology.

The Chairman: The discussion of Dr. Bredeck's paper will be given by Major E. M. Holmes, Jr., Medical Corps, U. S. Army.

Maj. E. M. Holmes, Jr.: Recent advances in the therapy of venereal diseases through the use of penicillin has undoubtedly influenced the epidemiology of syphilis and gonorrhea. What the future holds should be of interest. With syphilis being treated in 12 days as contrasted with the former 2-year schedules under arsenical therapy, infectiousness can be more easily controlled and the period of infectiousness materially reduced. With penicillin therapy being established in the treatment of gonorrhea, the incidence and, in turn, the period of infectiousness of the disease should be more easily reduced.

The epidemiologist has always been limited by, and of necessity followed, the advances in clinical medicine. Persons interested in the epidemiologic aspect of these diseases are aware of the results achieved in the control of syphilis through arsenical and bismuth therapy. Recently reports have indicated that there has been a decrease in the incidence of syphilis and that gonorrhea has increased. The decrease in the incidence of syphilis can to a large degree be attributed to the fact that we have had satisfactory methods of treatment for many years, and that through treatment we have been able to reduce infectiousness. In gonorrhea we have not had a satisfactory drug or treatment system prior to the use of the sulfonamides, and until the recent use of penicillin infectiousness with gonorrhea has been difficult to control.

If we are to eradicate the reservoir of infection existing in all communities in the United States, it is necessary that we adhere to basic public health principles. It is essential that our case-finding methods be reemphasized, and that our facilities for case investigation be made adequate. The prompt investigation of the sexual contacts of individuals with primary and secondary syphilis of less than one year's duration and the investigation of the contacts of all cases of gonorrhea is essential. We should keep in mind the fact that case finding per se is not our primary objective, but that our real objective is to provide treatment, and in turn to control infectiousness. If this is remembered and our efforts in case findings are directed toward infectious syphilis and gonorrhea much will be accomplished. Selection in case finding should be emphasized as much as we formerly emphasized selection in case holding, for our primary objective is to bring the suspect to examination and treatment, if such is found to be necessary, and thus to sterilize the infectious carriers.

The Chairman: The next paper this morning will be on biologic false positives by Dr. Hans Neurath of Duke University.

FALSE POSITIVE REACTIONS IN THE SEROLOGY OF SYPHILIS [1]

HANS NEURATH
Department of Biochemistry
Duke University School of Medicine
Durham, N. C.

It has been increasingly recognized in recent years that a positive serologic reaction for syphilis does not necessarily prove a syphilitic infection but that it may be elicited by a number of etiologically unrelated diseases, or even may occur in apparently normal individuals. In view of the grave nature of an unattended infection on one hand, and of the more or less arduous treatment

[1] The work described in this paper was done under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Duke University.

This work has been carried out at Duke University, School of Medicine, by a group of investigators which includes, H. W. Craig, E. Volkin, Drs. G. R. Cooper, J. O. Erickson, F. W. Putnam, D. G. Sharp, A. R. Taylor, and J. W. Beard. This project has been rendered possible by the unfailing cooperation on the part of Dr. J. E. Moore, Chairman of the Subcommittee on Venereal Diseases of the Committee on Medical Research, Lt Col. Charles R. Rein of the Army Medical School, and Dr. Herbert Lund of the City Hospital, Cleveland, Ohio. Serum specimens have been obtained from several Army General Hospitals through Brig. Gen. Hugh J. Morgan and Lt. Col. Rein, from the Naval Medical School through Capt. O. A. Smith, from civilian hospitals through Dr. J. E. Moore and Dr. Paul Rosahn, from the United States Public Health Service, Durham, through Dr. Samuel Fisher, and from the clinics of Duke Hospital through Dr. J. L. Callaway.

and its social stigma on the other, these so-called false positive reactions place an unprecedented burden of responsibility on clinicians and serologists alike.

The list of diseases recognized as apt to produce positive serology is impressive. It ranges from such tropical diseases as leprosy, kala-azar and malaria to the more commonly occurring afflictions of measles, glandular fever, virus pneumonia and upper respiratory infections in general. Likewise transitory positive reactions may occur following smallpox vaccination, while with apparently normal individuals, they may persist over a period of several months or even years. Although only a small fraction of positive reactions may be genuinely false, the total incidence is sufficiently frequent to be a matter of concern for public health. With the large number of routine serologic tests performed by the armed forces, and the mounting occurrence of diseases which may elicit false positive reactions, the problem has assumed sufficient military importance to induce the Committee on Medical Research of the Office of Scientific Research and Development to initiate in several institutions research projects on the differentiation between true and false positive reactions in the serology of syphilis.

The past years have witnessed the development of several so-called "verification tests" which purportedly "verify" a syphilitic or false positive reaction. Despite the wide application they have found, these tests are open to considerable criticism. They are based on empirical modifications of standard serologic procedures rather than on chemical or immunologic evidence. Proof of validity, by application to a statistically significant number of known syphilitic and false positive serums, has not been established for any one of these verification tests.

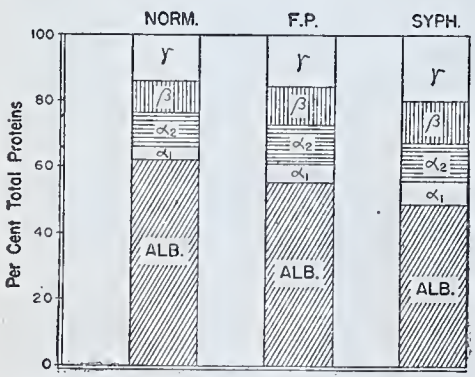
The present contribution describes preliminary data obtained in the course of an investigation which was designed to detect by chemical or immunologic methods, differences in the reactive antibodies of syphilitic and false positive serums.

The main object of the present investigation has been to determine whether false positive reactions are due to the presence of antibodies which, although serologically related to those present in truly syphilitic serums, are sufficiently distinct to provide, on the basis of their chemical or physical characteristics, a serologic method of differentiation.

Experimental approach to the problem is rendered difficult by two main factors: (1) The lack of a specific spirochetal antigen of human strain has compelled reliance on empirical complement fixation and flocculation reactions with nonspecific antigens, i.e. beef heart extract. Though the preparation of these antigens has been standardized, their chemical purity leaves much to be desired. (2) While there is a definite clinical base line for the identification of syphilitic serums, there is none for so-called false positive serums. Accordingly, we have accepted as syphilitic specimens those for which there was unequivocal clinical evidence for infection, whereas the group of allegedly false positive specimens may have included some genuinely syphilitic serums.

It will be recalled that blood serum contains a variety of protein components which, depending on their physical and chemical properties, are commonly designated as albumins and globulins. Anti-

bodies are associated exclusively with the serum globulins and may be separated from them, in relatively pure form, by specific serologic methods. The isolation of such purified preparations is desirable, and often essential, for an investigation of the behavior and properties of specific antibody systems. However, even in high titer syphilitic serums, the antibodies, sometimes also referred to as Wassermann antibody or reagin, constitute such a minute fraction of the total globulins, that their presence can hardly be demonstrated by physical or chemical methods. While Davis and Kabat have isolated the Wassermann antibody by specific flocculation with lipoidal antigen, followed by dissociation of the floccules with 15 percent saline, extremely low recovery of the resulting product, even from strongly active serums, precludes the application of this specific method to the present problem. As a substitute for a specific method, we have attempted to determine the distribution of the Wassermann antibody between the various serum globulins. However, since disease generally causes a more or less profound change in the quantitative distribution of the individual serum proteins, which as an approximation, may be expressed in terms of A/G ratios, it appeared necessary to determine first whether in syphilis, like in other diseases, there is a change in the serum protein patterns characteristic of the disease. Accordingly, comparative measurements have been performed of three groups of human serums, i.e. normal, syphilitic, and false positives.



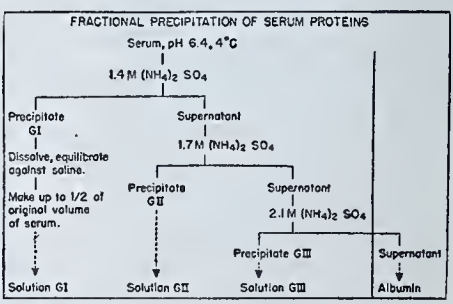


FIGURE 1.—*Diagramatic representation of the distribution of the serum proteins in normal, syphilitic, and false positive serums.*

FIGURE 2.—*Fractional precipitation of serum proteins with ammonium sulfate.*

Electrophoretic analyses were made on 13 normal, 25 syphilitic, and 45 biologic false positive serums. The serums from patients with syphilis differed markedly from normal serums in exhibiting decreased albumin and increased gamma globulin contents. The difference was in both relative and absolute amounts. Biologic false positive serums from presumably normal individuals showed differences from normal serums which were qualitatively similar to those of syphilitic serums but of considerably smaller magnitude. However, biologic false positive serums from individuals known to have disease other than syphilis gave findings essentially like those obtained with syphilitic serums.

Physical separation and isolation of the individual serum globulins by fractional precipitation with salts, under controlled conditions, followed by quantitative serologic analysis of the isolated

fractions, provided a practical and expedient means for determining the distribution of the Wassermann antibody between the various fractions. The method of fractionation is outlined schematically in figure 2.

FRACTIONATION OF SYPHILITIC SERA

A. High Titer

Serum	Fraction	Wasserm.	Mazzini	Kline	Kahn
No. 45	Serum	512		48	24
	GI	140		14	0
	GII	28		10	3
	GIII	3		2	2
	Total G	171		26	5
No. 92	Serum	256		96	128
	GI	128		32	32
	GII	64		16	24
	GIII	0		0	0
	Total G	192		48	56
No. 104	Serum	384		384	192
	GI	18		188	2
	GII	64		64	64
	GIII	0		3	12
	Total G	82		255	78
No. 50	Serum	1024		64	1024
	GI	64		24	24
	GII	192		24	48
	GIII	48		12	12
	Total G	304		60	84

FRACTIONATION OF SYPHILITIC SERA

B. Low Titer

Serum	Fraction	Mazzini	Kline	Kahn
No. 63	Serum	7	7	3
	GI	1	1	0
	GII	1	1	1
	GIII	0	0	0
	Total G	2	2	1
No. 140	Serum	2	2	0
	GI	±	±	0
	GII	0	0	0
	GIII	0	0	0
	Total G	±	±	0
No. 158	Serum	7	2	15
	GI	0	0	2
	GII	2	0	7
	GIII	0	0	0
	Total G	2	0	9
No. 166	Serum	6	3	4
	GI	1	0	0
	GII	1	0	0
	GIII	0	0	0
	Total G	2	0	0
No. 172	Serum	18	4	16
	GI	3	0	3
	GII	7	0	6
	GIII	0	0	0
	Total G	10	0	9

FIGURE 3.—*Distribution of serologic activity between the globulin fractions of high-titer syphilitic serums.*

FIGURE 4.—*Distribution of serologic activity between the globulin fractions of low-titer syphilitic serums.*

The isolated globulins have been designated, in order of precipitability by increasing concentration of ammonium sulfate, as GI, GII and GIII, whereas the supernatant solution remaining after precipitation of GIII was considered to contain crude "albumin." This method, although it does not yield chemically pure fractions, offered the advantage of at least partial purification of reagin, and further, of concentrating the activity to any desired degree, by concentration of the globulin fractions. The method has been applied to some 200 syphilitic and false positive serums, and the results of these analyses are shown in the following figures.

Figure 3 illustrates for a representative group of high titer syphilitic serums the distribution of the serologic activity between the three globulin fractions, as determined by the Wassermann, Mazzini, Kline diagnostic, and Kahn quantitative standard methods. The data are given in units of titer, corrected to the concentration of the fractions in the original serum. It may be seen that fractions GI and GII are considerably more active than GIII and that the sum of the titer of the isolated fractions tends to be less than the titer of the parent serum. Both of these effects become accentuated in low titer syphilitic serums, as may be seen from figure 4.

It should be emphasized at this point that since experience has shown false positive serums to be only weakly reactive, low titer syphilitic serums should be employed for comparative analyses.

A similar analysis of false positive serums led to the curious but elucidative result that the sum total of the titer of the isolated globulins exceeds considerably the titer of the whole serum.

FRACTIONATION OF FALSE POSITIVE SERA

Serum	Diagnosis	Fraction	Wasserm.	Mazzini	Kline	Kahn
No. 68	Normal ?	Serum	0		0	0
		G I	AC		26	36
		G II	AG		4	6
		G III	0		0	0
		Total G	?		30	32
No. 73	Normal ?	Serum	24		0	0
		G I	AC		0	0
		G II	AC		0	26
		G III	0		0	0
		Total G	?		0	26
No. 82	Leprosy	Serum	0		0	0
		G I	0		0	0
		G II	86		0	28
		G III	0		0	0
		Total G	86		0	28
No. 134	Virus pneumonia	Serum	0	2	2	2
		G I	AC	0	0	0
		G II	2	1	5	20
		G III	0	0	0	0
		Total G	?	1	5	20
No. 151	Normal ?	Serum	0	0	2	0
		G I	AC	4	10	18
		G II	AC	0	4	8
		G III	0	0	0	0
		Total G	?	4	14	26

FIGURE 5.—*Distribution of serologic activity between the globulin fractions of false positive serums.*

Indeed, several of the serums listed in this figure, as well as numerous other ones not shown here, happened to be entirely seronegative at the time the blood was drawn, whereas elimination of the albumin, by fractional precipitation of the globulins, yielded more or less strongly active products. This is in contrast to genuinely normal, seronegative serums where the globulins, no matter how concentrated their solutions, are usually devoid of any serologic activity. It may be interjected at this point, that certain animal serums, such as those of the horse, behave in this respect much like false positive human serums.

This finding of an increase in reactivity following removal of the albumin is of considerable practical and theoretical significance: Clinicians and serologists are often puzzled by so-called "doubtful reactions," i.e. reactions which are too weak to be considered unambiguously as genuinely positive. They are apt to occur in the very instances where in the absence of a clear-cut clinical diagnosis, heavy reliance has to be placed on the serologic findings. As will be shown in subsequent figures, these doubtful reactions may be resolved into genuinely false positive reactions if the activity of the isolated globulins is increased, or else into presumably syphilitic reactions if the globulins are seronegative.

The theoretical implication of this phenomenon lies in the fact that in contrast to most serologic systems, the reaction between lipoidal antigen and false positive antibody is influenced by the presence of nonspecific serum proteins, particularly by some component associated with serum albumin. This has been confirmed experimentally in that addition of the crude human serum albumin to the globulin fractions of false positive serums, causes complete inhibition of their activity. With syphilitic globulins, however, addition of serum albumin has little effect. The data shown in the following figures substantiate this conclusion.

Representative data of the inhibitory effect of crude albumin on false positive globulins are shown in figure 6.

For comparison the results of similar experiments performed with low-titer syphilitic globulins are shown in figure 7.

INHIBITION OF SEROLOGICAL ACTIVITY OF FALSE-POSITIVE GLOBULINS BY HUMAN SERUM "ALBUMIN"

Fraction	Diagnosis		Mazzini	Kline	Kahn
135 GI	Lupus eryth. diss.	Control	4	2	12
		+Albumin	0	0	0
151 GI	Normal	Control	4	16	24
		+Albumin	0	0	0
130 GI	Normal	Control	0	16	24
		+Albumin	0	0	0
134 GII	Virus pneumonia	Control	0	0	48
		+Albumin	0	0	0
139 GI	?	Control	12	4	18
		+Albumin	0	0	0
202 GI-II	Normal	Control	0	7	0
		+Albumin	0	0	0
82 GII	Leprosy	Control	24 (w&m.)	0	6
		+Albumin	0	0	0

EFFECT OF HUMAN SERUM "ALBUMIN" ON SYPHILITIC GLOBULINS

Fraction		Mazzini	Kline	Kahn
157 GII	Control	16	4	8
	+Albumin	9	1	3
179 GII	Control	1 1/2	1/2	1 1/2
	+Albumin	3	1/2	2 1/2
185 GII	Control	4	0	4
	+Albumin	3	0	3
186 GII	Control	1	0	1
	+Albumin	1	0	1
266 C	Control	3	2	3
	+Albumin	3	1	3
227 C	Control	11	8	15
	+Albumin	9	8	10
267 C	Control	4	1 1/2	3
	+Albumin	4	0	1 1/2

FIGURE 6.—*Inhibition of serologic activity of globulins derived from false positive serums by crude human serum albumin.*

FIGURE 7.—*Effect of crude human serum on syphilitic globulins.*

It is of interest to note that human albumin not only inhibits flocculation of false positive globulins by lipoidal antigen, but that it is also capable of redispersing the floccules, but not the floccules of true syphilitic serums when subsequently added to them.

I shall not discuss the numerous experiments which we have performed in an attempt to identify the chemical nature of this inhibitor. Suffice it to state that it is associated with the albumin fraction, though crystalline albumin itself is devoid of inhibitory activity. The inhibitor is species specific and does not seem to occur in animal serums. It is heat-stable and remains active after coagulation and redispersion of the albumin by various means. Further work on its identification is in progress.

The differential behavior of syphilitic and false positive globulins toward the same lipoidal antigen suggests that different antibodies are involved in these two groups of serums. Accordingly, it was deemed of interest to search for other criteria by means of which these two antibodies may be told apart. Antibodies, like most biologically active proteins, become inactivated when heated above a certain temperature. The susceptibility of syphilitic and false positive antibodies to heat inactivation has been studied by heating the serums, or the isolated globulins, for 20 minutes at temperatures ranging from 56° to 66° C. The results of representative measurements on the heated samples are shown for syphilitic fractions of varying initial titer in figure 8.

It may be seen that there is a gradual decrease of titer with increasing temperature and that temperatures of 66°C or higher are required for complete inactivation.

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HEAT STABILITY TESTS
Syphilitic Fractions

Sample	Dilution		Temperature 56°	60°	62°	64°	66°
Pooled GI	1:2	KL	16	8	4	4	2
		KN	24	16	12	4	2
No. 92 GI	1:7	KL	12	12	12	8	
		KN	12	12	16	16	
No. 92 GII	1:1	KL	48	48	48	48	
		KN	48	48	48	24	
No. 143 GI	1.5:1	M	10	10	7	6	
		KL	8	7	7	5	
		KN	12	7	6	4	
No. 143 GII	2:1	M	10	8	7	4	
		KL	12	9	5	3	
		KN	9	9	4	2	
No. 162 GII	3:1	M	9	8	7	4	
		KL	0	0	0	0	
		KN	7	6	5	*	

HEAT STABILITY TESTS
False Positive Fractions

Serum	Dilution		Temperature 56°	60°	62°	64°	66°
107 GI	3:1	KL	12	6	2	0	0
		KN	12	6	4	?	0
107 GII		KL	?	0	0	0	
		KN	24	0	0	0	
90 GI	1:2	KL	?	0	0	0	
		KN	8	0	0	0	
90 GII	1:1.5	KL	?	0	0	0	
		KN	18	0	0	0	
89 GII	4.7:1	KL	0	0	0	0	
		KN	12	10	7	0	
98 GII	2.7:1	KL	24	18	12	0	
		KN	0	0	0	0	
97 GII	2.7:1	KL	0	0	0	0	
		KN	16	4	0	0	
134 GII	2:1	M		Negative			
		KL					
		KN	28	20	4	0	
149 GII	2:1	M	7	4	1	0	
		KL	4	1	0	0	
		KN	5	2	0	0	
139 GII	3:1	M	8	8	4	0	
		KL	0	0	0	0	
		KN	8	8	0	0	

FIGURE 8.—*Heat stability tests on syphilitic fractions (M-Mazzini; KL-Kline; KN-Kahn).*
FIGURE 9.—*Heat stability tests on false positive fractions.*

Analogous experiments with false positive serums, or fractions, revealed a considerably greater susceptibility to inactivation by heat. As shown in figure 9 complete inactivation ensues at temperatures above 62°C. These effects appear to be independent of initial titer (within the limits of sensitivity of the serologic methods) and independent of the concentration of the globulins. Comparative heat stability measurements with some 50 syphilitic and false positive samples, respectively, have left us with the impression that the false positive antibody is less heat-stable than the syphilitic antibody, but an extension of this work to a much larger number of specimens is required to prove the validity of this conclusion.

Time does not permit a discussion of various other approaches that we have made toward the differential characterization of syphilitic and false positive antibody. It may be mentioned in passing that it has been possible to achieve a considerable degree of purification of the syphilitic antibody by adsorption from whole serums on freshly precipitated calcium phosphate. The adsorbed materials, containing antibody in addition to a fraction of all serum proteins, could be eluted from the calcium phosphate precipitate and then again subjected to fractional precipitation with ammonium sulfate. This procedure yielded, under optimum conditions, a solution which contained as little as 0.1 mg. of protein per cubic centimeter per 4 flocculation units. A limited number of experiments has shown that while with syphilitic serums of high, moderate, or low titer, most of the antibody is adsorbed on the calcium phosphate, the antibodies contained in false positive serums are not precipitated under these conditions.

A more expedient and practical method of refinement has been developed more recently, based on the fact that serum globulins may be separated in vitro into two fractions, one of them becoming insoluble when the salt concentration is sufficiently decreased and the pH of the solution adjusted to a proper level. Since the syphilitic antibody has been found to be associated preponderantly with the gamma globulin which, of all globulin components, yields the largest amount of water-insoluble material, we have chosen such

conditions of pH and salt concentration as to yield a maximum amount of water-insoluble gamma globulin. This precipitate may be readily dispersed in appropriate buffer solutions and used for serologic analysis. This method, the details of which are on file with the Committee on Medical Research, is extremely rapid and simple, and requires hardly more than 6 cc. of serum, a trained technician, a tank of CO_2, and a laboratory centrifuge. The isolated globulin fraction contains only about one-tenth of the total serum proteins but 60 percent or more of serologic activity. Again, with false positive serums the activity of the fraction is considerably higher than that of the parent serum, and is completely inhibited by serum albumin.

The results of such routine analyses on a series of malarial serums which gave doubtful serologic reactions are shown in figure 10.

SEROLOGICAL ANALYSIS OF MALARIA SERA

No.	Fraction	Conc.	Mazzini	Kline	Kohn
206	Serum	-	0	0	0
	Globulins	2x	2 1	2 2 1 0	1 1 1 ± 0
	Globulins + Alb.	2x	0	0	0
207	Serum	-	0	0	0
	Globulins	2x	1	4 2 1	4 2 1 ±
	Globulins + Alb.	2x	0	0	0
209	Serum	-	0	0	0
	Globulins	2x	2 1 ±	2 1 ±	4 4 2 1 ±
	Globulins + Alb.	2x	0	0	0
221	Serum	-	0	0	0
	Globulins	1.5x	0	±	1 ± ± 0
	Globulins + Alb.	1.5x	0	0	0
223	Serum	-	0	0	0
	Globulins	1.5x	1 ± 0	4 3 2 ± 0	1 ± ± 0
	Globulins + Alb.	1.5x	0	0	0

SEROLOGICAL ANALYSIS OF ALLEGEDLY FALSE POSITIVE SERA FROM "NORMAL" INDIVIDUALS

No.	Fraction	Conc.	Mazzini	Kline	Kohn	Type
199	Serum	-	0	0	0	Neg.
	Globulins	2x	0	0	0	
200	Serum	-	±	±	1 ±	
	Globulins	2x	±	0	1 1 ±	F.P.
	Globulins + Alb.	2x	0	0	0	
201	Serum		1 ±	1	1 ±	
	Globulins	2x	1 ±	1	1	Syph.
	Globulins + Alb.	2x	±	±	1	
202	Serum		0	1	0	
	Globulins	2x	0	3 2 1 0	0	F.P.
	Globulins + Alb.	2x	0	0	0	
212	Serum	-	±	0	0	
	Globulins	2x	1	1 ±	1 ±	Incon.
	Globulins + Alb.	2x	±	±	0	
321	Serum	-	1 ±	1 ±	2 1 0	
	Globulins	2x	1	2 1 ±	2 1 ±	F.P.
	Globulins + Alb.	2x	0	0	0	
331	Serum	-	2 1 ±	1	1 ±	
	Globulins	2x	1 ±	1	1 ±	Syph.
	Globulins + Alb.	2x	2 1 0	0	1 ±	

FIGURE 10.—*Serologic analyses of malaria serums.*

FIGURE 11.—*Serologic analyses of allegedly false positive serums from normal individuals.*

The interpretation of these data is the same as that of those shown in preceding figures for globulin fractions prepared by the ammonium sulfate method. Similar experiments with allegedly false positive serums from apparently normal individuals are shown in figure 11.

Here, according to our interpretation, some of the specimens are completely seronegative, and presumably normal, some are false positive, and some syphilitic.

In conclusion, I shall integrate the data presented and discuss the promise they offer toward a solution of the problem of the differential serodiagnosis of syphilitic and false positive serums.

1. We have attempted to determine, by empirical methods, whether the antibody present in false positive serums differs from the truly syphilitic antibody in chemical physical or serologic behavior, and whether such differences as may exist lend themselves to the development of a differential serodiagnostic method. This approach is rendered difficult by the lack of a specific antigen and for want of a clinical base line for false positive serums. Further, since in both groups of serums the antibody constitutes a minute fraction of the total proteins, reliance had to be made on nonspecific methods of purification, based on separation of the individual

globulins by two methods: (a) fractional precipitation with ammonium sulfate, and (b) precipitation by a more rapid and expedient method based on the insolubility of some globulin components in solution of low salt concentration. Although the resulting products contain a large amount of serologically inert proteins, crude albumin which inhibits the activity of false positive globulins, has been eliminated by these methods. Increased reactivity of the isolated globulin, relative to the whole serum, has been found to be characteristic for false positive serums. With syphilitic serums, these methods of separation lead to an apparent decrease in reactivity.

2. Addition of crude human albumin to false positive globulins causes inhibition of their activity as well as redispersion of the specific floccules. No such effects were noted with syphilitic globulins.

3. False positive serums, or fractions, are more susceptible to heat inactivation than syphilitic serums or fractions.

4. Precipitation with calcium phosphate lends itself to the further purification of syphilitic antibody whereas false positive antibodies are not affected under similar conditions.

5. Syphilitic and false positive serums appear to differ also in the quantitative distribution of the serum proteins, as revealed by electrophoretic analysis; however, individual variations within each group are too great to render this method of practical value.

OBSERVED DIFFERENCES BETWEEN SYPHILITIC AND FALSE POSITIVE SERA

Syphilitic	False Positive
1. Globulins less active than whole serum	Globulins more active than whole serum
2. Serum albumin without effect on globulins	a) Serum albumin inhibits serological activity of globulins
	b) Serum albumin redisperses floccules
3. Serum and globulins active above 62° C	Serum and globulins inactive above 62° C
4. Antibody absorbed on colloidal calcium phosphate	Antibody not absorbed on colloidal calcium phosphate

FIGURE 12.—*Observed differences between syphilitic and false positive serums.*

Chemical and immunologic considerations demand that before any verification procedure can be claimed to have validity, or even reality, it must be demonstrated that the antibodies elicited in syphilitic and false positive serums, respectively, are chemically or serologically different. Further, any such verification technic must be based on established differences in the properties or reactivities of the antibodies rather than on trial and error modifications of standardized serologic methods. I wish to emphasize at this point that we are not prepared to make any promise or claim that the data presented today will eventually lead to a practical and specific method of differentiation. I do believe, however, that the experiments described have been performed on a sufficiently large number of specimens to indicate that the antibodies in false positive serums depart in various significant respects from the behavior of the Wassermann antibody of syphilitic serums.

I wish to acknowledge the splendid cooperation of Rein and his staff which has enabled a continuous exchange of materials and data. While our initial hopes of establishing a correlation

between the selective inhibition of syphilitic serums by raw human serum, as described by Rein, and the inhibition of false positive serums by albumin, as observed here, have not fully materialized, we have shared the alternating moments of elation and disappointment which always accompany research on an elusive problem such as the present one.

The Chairman: Dr. Neurath's paper will be discussed by Dr. R. C. Arnold, of the Public Health Service Venereal Disease Research Laboratory, Staten Island, N. Y.

DISCUSSION

R. C. ARNOLD, *Surgeon,*
United States Public Health Service
Associate Director, Venereal Disease Research Laboratory
Staten Island, N. Y.

Undue emphasis has not been placed on the occurrence of false positive reactions in the serology of syphilis. The diagnostic and quantitative serologic procedures give positive reactions in syphilis but also may produce positive reactions in certain nonsyphilitic conditions. The clinician and health officer may expect to encounter an increase in this type of serodiagnostic problem when the members of the armed services, who have had various vaccination procedures as well as tropical and acute infectious diseases, return to civil life. Until such time as the work of Dr. Neurath and other investigators gives a laboratory solution to the question of nonspecific reactivity, the diagnosis of syphilis remains a clinical problem.

A patient with nonspecific serologic reactions may require several weeks or even months of continued clinical observations and laboratory studies before the final diagnosis can be established. A review of the anamnestic record may reveal the details of a previously denied venereal infection. The detailed physical examination should include special studies of the cardiovascular, cutaneous, skeletal, and nervous systems. Members of the immediate family or nonrelated sexual contacts should be consulted with case-finding methods. The serologic base line established with the approved qualitative and quantitative tests may be used to gage future serologic trends. Spinal fluid examinations should be rechecked if discrepancies are evident in the clinical and laboratory reports. X-ray photographs may reveal abnormal conditions of the cardiovascular stripe, in the osseous structure, or heavy metal deposits in the gluteal muscles.

The clinical and laboratory data may not be adequate for making a definite diagnosis at first. The majority of nonspecific positive reactions usually revert to the seronegative phase within a few months. However the host mechanism for the production of reactive substances in the blood may need only a minimal stimulant to prolong the abnormal serologic reactivity. With a few nonsyphilitic patients the nonspecific positive reactions may persist for years. Unfortunately the diagnostic problem is complicated by a group of patients, especially females, who have developed a symptomless invasion of syphilis with the positive serologic results as the sole indicator of the disease. Provocative tests with arsenical

drugs do not yield fruitful results. Active antisyphilitic therapy should be deferred until the definite diagnosis of syphilis is confirmed. Except in pregnancy and early infectious syphilis, treatment may be deferred safely for several months during which time the majority of nonsyphilitic positive reactions will become negative. However, in a residual number of patients it may not be possible to establish a definite diagnosis with the available diagnostic methods.

The behavior characteristics of the globulin fractions, obtained from syphilitic and other serums, are most interesting phenomena. The results of the experimental study at this time indicate certain definitive patterns in various types of specimens. The development of a procedure for separating the components of blood serum and the testing of individual and composite fractions presents a new approach for differentiating syphilitic and nonsyphilitic specimens. The evaluation of clinical data and laboratory reports in certain patients are expected to present perplexing diagnostic problems for the clinician until a specific test is available which will prevent the unwarranted diagnosis of syphilis and which will shorten the prediagnostic periods of extensive investigation.

Dr. Neurath and his coworkers have had the courage to tackle one of the most baffling problems in the diagnosis of syphilis. Whether or not their method will afford the greatly needed answer, as it now gives promise of doing, the ultimate end of all such research must be one of benefit to the science of serology and to the clinician who calls it to his aid.

The Chairman: The next paper will be given by Dr. Richard A. Koch, in collaboration with Dr. Ray Lyman Wilbur of California.

Dr. Richard A. Koch: It is indeed a pleasure to have had the opportunity to assist Dr. Ray Lyman Wilbur, President of the American Social Hygiene Association, in the preparation of this paper. Dr. Wilbur sincerely regrets that he has been unable to be present at this meeting.

PROMISCUITY AS A FACTOR IN THE SPREAD OF VENEREAL DISEASE

RICHARD A. KOCH, M.D., *Chief, Division of Venereal Diseases,*
City and County of San Francisco, Department of
Public Health

and

RAY LYMAN WILBUR, M.D., *President,*
American Social Hygiene Association

INTRODUCTION

Venereal diseases are one of the greatest preventable human tragedies. The reason we fail to conquer them is our prudery and our failure to face the over-all problems, their causes, and background. The sex urge is as fundamental as that of hunger and thirst, and in our sensate society that urge has led to promiscuity.

Sexual promiscuity is the most vital factor in the spread of venereal diseases. If sexual promiscuity were eliminated from our national life, venereal disease would as a natural course disappear from our State without the necessity of medical intervention. Venereal disease control is concerned inseparably with the physical

and social aspects of our national life. It is thus concerned with the moral fiber of the community, the church, the home, and with those factors and agencies, official and nonofficial, which strengthen that moral fiber, as well as with those factors that tend to weaken it. We must remember that we cannot control the morals of people by legislation, but we certainly can control the environment of youth. Venereal disease control is, therefore, related to church activity, school activity, parent-education programs, youth agencies, recreational activities, law enforcement, protective care of girls and boys, training in leadership, and a long range public health educational program.

This diversity of factors related to the control of venereal diseases is not characteristic of the venereal diseases alone. The control of typhoid fever is not exclusively a medical problem. Its control is related to the control of the sanitary environment and to the vast ramification of engineering feats that are necessary to effectuate this control. The control of tuberculosis is not alone a medical problem. Its control is related to the provision of improved housing conditions through slum clearance; to the provision of adequate parks and playgrounds; to the development of a general concept of a healthy social life providing sufficient recreation, freedom from overcrowding, balanced nutrition, and an understanding of family hygiene. There are many nonmedical factors also used in the control of malaria, yellow fever, cholera, dysentery, plague, and other communicable diseases.

Unquestionably, venereal disease control is of a more personalized nature than the control of the other communicable diseases. Perhaps for this reason the venereal diseases have, to a large degree, defied control. It is for us to recognize the diversity of the problems involved and to effectuate programs directed towards their solution.

The nonmedical problems related to venereal disease control are those that relate tc sexual promiscuity. Promiscuity in the male has always been more or less condoned as long as such promiscuity was not blatantly forced upon the public. Just as the satisfaction of hunger and thirst is commercialized by the food establishments with the preparation of attractive articles of food, so also is the satisfaction of the sex urge likely to be commercialized. Such commercialization, if the community permits, involves the establishment of houses of prostitution with the result that where such houses exist a high percentage of venereal disease is certain to be found. It has been shown that if commercialized prostitution is actively repressed, a decline in the incidence of venereal disease follows. Prostitution is, of course, a system intended to serve male promiscuity. It is intolerable in a democratic society.

In our past history, promiscuity of the female has not been accepted. We are only a few decades away from the days when a promiscuous woman would find her door painted with tar as the sign of disapproval of her moral looseness. If we attempt to trace the acute development of female promiscuity in contemporary times, we need search no further than World War I, when women gained more freedom outside the home, and the passage of the Nineteenth Amendment in 1920, when women gained the same political privileges and freedom held by men.

As a woman has become more prominent in the business world and has accepted greater freedom outside of the home, she has also to some degree accepted the same masculine freedom in relationship to sex. A few years ago the largest percentage of venereal disease came from prostitutes, but since the repression of commercialized prostitution the promiscuous girl has been left as the major source of venereal infection. Therefore, today the problem of venereal disease control is with the promiscuous girl and not the prostitute. Not only is this a wartime problem, but with the lowering of moral conduct and the loosening of old controls and safeguards, more and more, the promiscuous girl as the spreader of venereal disease will be a definite postwar problem.

Those who have worked in the field know that if ever venereal diseases are to be eradicated, the control must be related not only to medicine and public health but also to welfare, church, law enforcement, education, and public understanding, and must be supported by all agencies, private and governmental.

The solution of the problem of promiscuity does not lie in the hands of the medical profession. It will be corrected only by cultural changes in society. Surgeon General Thomas Parran has written (*1*) "It is my opinion that too often in the past health officers have neglected their direct medical responsibilities in controlling syphilis and have diluted their efforts by attempting to function in the whole field of social hygiene. The repression of prostitution is primarily the responsibility of the law enforcement agency. The teaching of sex hygiene is primarily the function of the parent and educator, secular, and religious. As a good citizen, the health officer should work wholeheartedly with both. As a public servant, he should do his own job and endeavor to coordinate it intelligently with both."

The official health agency, being directly concerned with the control of all communicable diseases, must act as a community catalyst in bringing about a public awareness of the over-all community problems pertaining to the dissemination of venereal diseases.

STATISTICAL ANALYSIS

We have found among 8,027 persons examined in a prewar serologic survey among labor unions in northern California (*2*) that the incidence of positive serologic findings among the employed was 3.7 percent, whereas among the unemployed it was 5 percent. In a summary of studies made from 1935 to 1940, Dr. Walter Clarke (*3*) reported syphilis was more prevalent in the relief (unemployed) groups than in the employed groups. We further found (*2*) in the northern California area group the incidence of positive serology to be 3.8 percent in the resident and 6.3 percent in the nonresident or transient, a difference of incidence indicating that those who live transient, migratory lives are more prone to promiscuity and have a higher incidence of syphilis than those who live a resident, nontransient life.

In the serologic examination of 14,354 new employees of a San Francisco war industry (table 1) which represent, in the large, a transient population, or a population which did not have its roots

deeply established in a communal environment, we have found 1,590 (11.1 percent) to have a positive serology; 685 (6.0 percent) whites and 905 (30.6 percent) Negroes. These statistics again illustrate the high incidence of syphilis among the relatively promiscuous transient. On the other hand, examination of 3,610 workers from the same industry before the introduction of large masses of migratory workers (table 1) showed 214 (5.9 percent) to have positive serologic reactions; 108 (3.7 percent) white and 106 (15.5 percent) Negro; thus again is illustrated the lower incidence of syphilis in the resident, less promiscuous class of our population. Further analysis of this table shows the low incidence of positive serology in our stable population.

TABLE 1.—*Serologic findings in employees of San Francisco industries*

		Total	Positive	Percentage
Serologic survey of permanent employees in 4 old-established San Francisco manufacturing firms	White	1,187	31	2.6
	Negro			
Total		1,187	31	2.6
Serologic survey of a San Francisco war industry prior to the employment of a large number of migratory workers	White	2,924	108	3.7
	Negro	686	106	15.5
Total		3,610	214	5.9
Serologic survey of the migratory workers employed by the above war industry	White	11,400	685	6.0
	Negro	2,954	905	30.6
Total		14,354	1,590	11.1
Serologic survey of employees in a transient war service	White	2,142	166	7.8
	Negro	859	256	29.8
Total		3,001	422	14.1

Occupational status is related to social stability and the establishment of a permanent home. In various industrial surveys in the San Francisco area (*4*), out of a total of 7,147 workers whose occupation was known the incidence of positive serologic reaction in percentages was as follows:

Unskilled laborers	5.0 percent
Semiskilled laborers	4.6 percent
Skilled laborers	3.7 percent
Office workers	4.3 percent
Professional workers	1.1 percent

The incidence of syphilis decreased with increase of employment stability.

The Psychiatric Service of the San Francisco City Clinic offers figures related to promiscuity. Patients referred to this service in 1943 were those who had been interviewed by public health nurses and doctors and found to be sexually promiscuous, not prostitutes, and generally under 22 years of age. Promiscuity was

defined as sex delinquency of a noncommercial character. It included a girl who might receive clothes, meals, a gift, or even money, if such returns did not constitute her conscious reason for resorting to sexual promiscuity, and who did not confine her attention to one or two male friends.[1]

Of 168 patients on whom complete psychiatric case studies were done, 63 percent came from currently broken homes; 83 percent reported familial conflicts, some of whom were at the point of open breaks with their families, while others blamed their families for their situation, there being a wide range of difficulties between the patients and their parents. An analysis of 158 of these 168 patients whose records were known showed that 18 percent had been in correctional schools or had juvenile court experience. Almost all of these 168 patients indicated they had been affiliated with some religious group in childhood. A large majority had ceased attendance at Sunday school or church before or during adolescence. Most of these patients did not adhere to any form of organized religion at the time of the interview. Many of the patients who claimed affiliation with a church had recently come from small communities where the church was a social and recreational center as well as a place of worship. Statistics on 163 patients of the Psychiatric Service show 39 (23.9 percent) claimed no present church affiliation, although almost all of these had had some previous church or Sunday school affiliation. The chief recreations of this group of patients studied by the psychiatric service were such commercialized recreations as frequenting bars, dance halls, and cheap movies, reading "pulp" romances and detective stories, and frequenting beach concessions habitually as a means of meeting men.

The women examined at the San Francisco Separate Women's Court from March 1943 through September 1944 offer important case-study statistics (table 2).

TABLE 2.—*Statistical evaluation and classification of 1,402 cases appearing before the San Francisco Separate Women's Court, March 1943 through September 1944*

	Total cases investigated	Prostitutes	Promiscuous	Alcoholics	Drug addicts	Repeat investigations	Total investigations
Number	1,402	311	751	283	57	278	1,680
Percent	100	22.2	53.5	20.2	4.1	----------	----------

Classification of the women by the social service department shows that 311 (22.2 percent) were prostitutes, 751 (53.5 percent) were promiscuous women, 283 (20.2 percent) were alcoholics, and the remainder 57 (4.1 percent) were classified as drug addicts. For the purpose of this classification, prostitutes were defined as women who required pay for their sexual act; promiscuous women, as previously mentioned; alcoholics, as those who were routinely sexually promiscuous due to the effects of alcohol or who were

[1] This definition conforms with the definition of promiscuity in the report of the Committee on Sex Delinquency in Young Girls, which met in New York, Nov. 23-24, 1942, at the invitation of the American Social Hygiene Association, Bascom Johnson, Chairman.

so in order to procure alcohol, and drug addicts, as those who were sexually promiscuous due to the effect of drugs or who were so in order to procure drugs.

This study shows the important place the promiscuous woman now takes in venereal disease control, especially when it is pointed out that about 60 percent of all venereal disease reported in San Francisco is contacted through the media of bars and taverns.

Table 3 illustrates part of the social background of the women appearing before the San Francisco Separate Women's Court. These women were referred to the Court following arrest for alleged vagrancy or prostitution.

TABLE 3.—*Tabulation of home life, religion and record of arrests for 1,402 women appearing before the San Francisco Separate Women's Court*

		Number	Percent
Broken home		794	56.7
Home with parents		382	27.2
Unknown		226	16.1
Total		1,402	100.0
Church affiliation		1,184	84.5
No religion		218	15.5
Total		1,402	100.0
Stated as active church affiliation	22		24.5
Stated as inactive church affiliation	68		75.5
Total	90		100.0
Record of previous arrest		635	45.3
No known record		742	52.9
Unknown		25	1.8
Total		1,402	100.0

A broken home or an unhappy home background was defined as any breaking up of the solidarity of the home by (1) death of one or both parents when the child was 18 years of age or under; (2) divorce or separation of the parents; (3) removal of the child from home, i.e., placed in boarding school, work home, foster home, etc.; (4) illegitimate child of mother.

It is interesting to note the concurrently similar findings of Dr. Rachlin (*5*) who reports 52 percent of 249 women studied at the Midwestern Medical Center in St. Louis, Mo., came from broken homes.

The San Francisco Separate Women's Court group showed that 84.5 percent stated some religious affiliation, but in the majority of instances this was only an expression of faith; detailed analysis of 90 of these patients showed 68 (75.5 percent) to be religiously inactive.

The large number of first offenders, 742 (52.9 percent), is of importance. This figure coincides with the number of promiscuous women, 53.5 percent, as shown in table 2. This is also a reflection

of the social condition of our times.

Evaluation of the mental level of women appearing before the Separate Women's Court is of importance in an adequate consideration of the problem of promiscuity. These figures are a result of the study of Dr. Mary C. Van Tuyl, Separate Women's Court psychologist. The tests used were the Otis Beta B group test and Wechsler individual test adult scale, as we were concerned with the best measure of intelligence quotient for the particular patient.

Chart I shows graphically the mental level by race for 553 women appearing before the Separate Women's Court from Feb. 21 to Sept. 22, 1944. It is of interest to point out that 61 percent of the white cases and only 34 percent of the Negro cases fell within the grouping "dull normal and normal." It should be further pointed out that in the white cases 67 percent are above the defective and borderline defective level. Of the total cases, 57.8 percent are of a mental level of dull normal or better, the evidence thus showing the subjects, on a basis of intelligence, to be amenable to redirectional care.

Chart II shows the percent distribution of infection within the various mental level groupings. It is of interest to note the small fluctuation of venereal disease incidence in the various mental levels of the white women; while this fluctuation is more marked in Negro women, the difference is not great. One might, therefore, consider that mental level was not necessarily related to the incidence of venereal disease in this class of patient.

Chart III relates the mental level groups found in the women at the Separate Women's Court with the expectancy curve found in a normal population as reported by Wechsler (*6*). According to the expectancy curve, 50 percent of a normal population falls within the limits of the normal mental level (91 to 110 IQ); in our population only 32 percent of the total cases fell within this normal range. This figure is 18 percent below the normal expectancy. The incidence of borderline defectives in our group was 21.3 percent above the expectancy in the normal population.

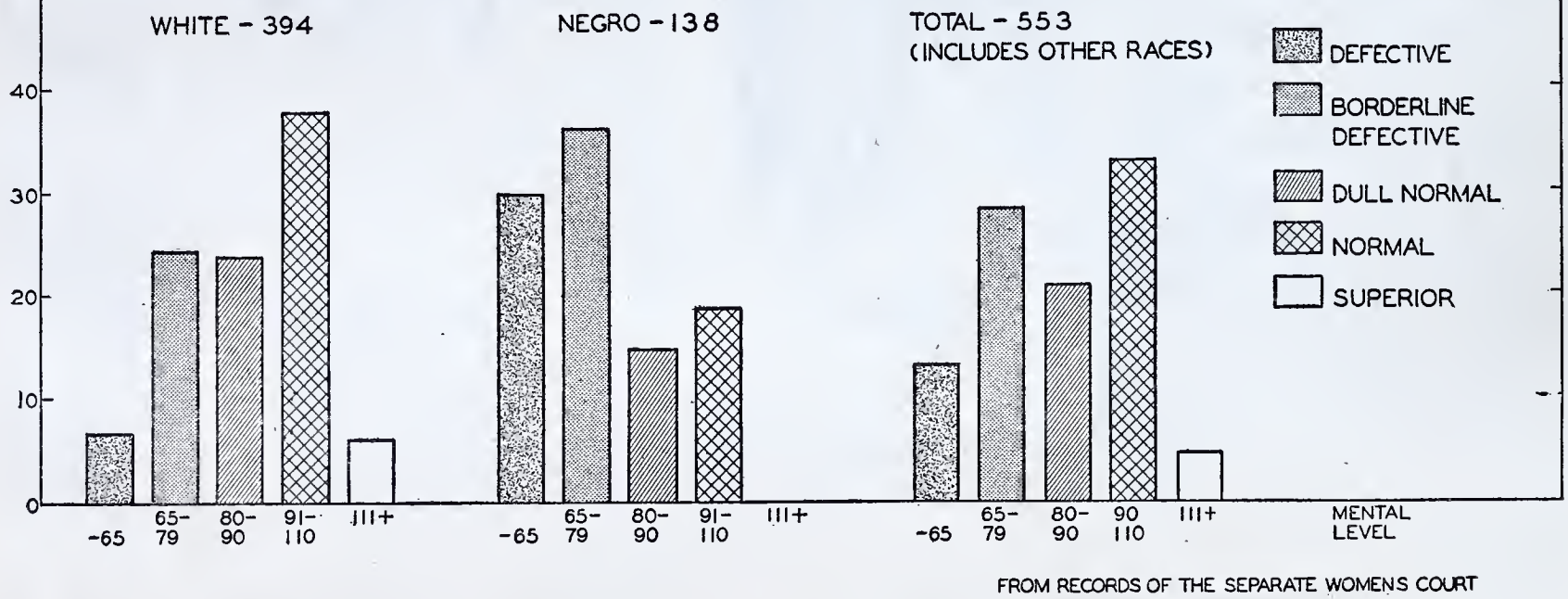
These figures tend to point out that the problem of promiscuity is to some degree related to low mental intelligence, as compared to the average population, but the evidence is not strikingly conclusive. The group in the main, from a mental level point of view, is amenable to redirectional treatment.

GENERAL CONSIDERATIONS

The medical profession now has new and lethal weapons with which to combat venereal disease. While the old weapons were effective, the new ones are likely to be even more so. We should be forewarned, however, that penicillin is not likely to be a panacea for the cure of both syphilis and gonorrhea. As the sulfonamides

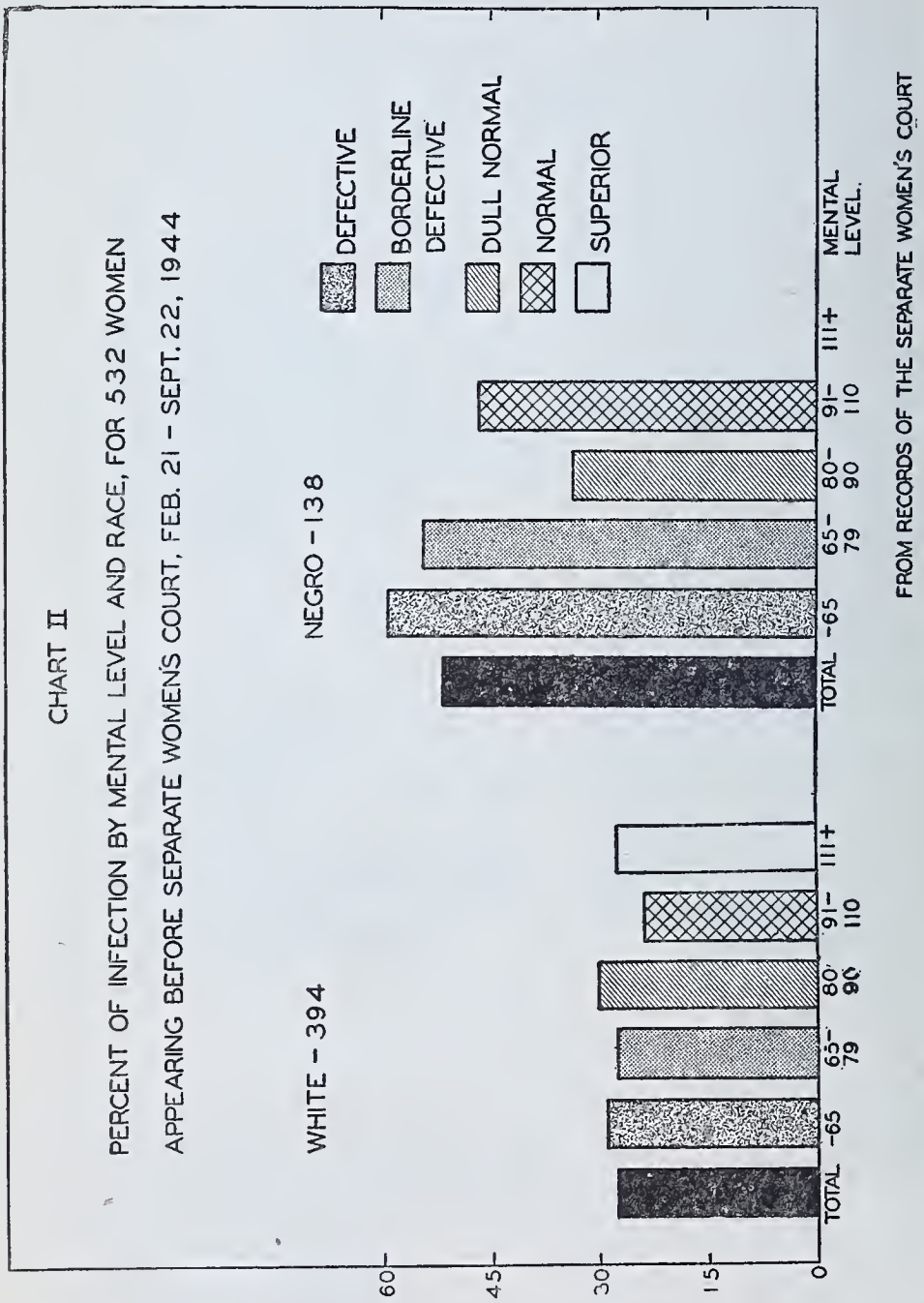
CHART I

DISTRIBUTION OF MENTAL LEVEL BY RACE FOR 553 WOMEN APPEARING BEFORE SEPARATE WOMEN'S COURT, FEB. 21 - SEPT. 22. 1944



FROM RECORDS OF THE SEPARATE WOMENS COURT

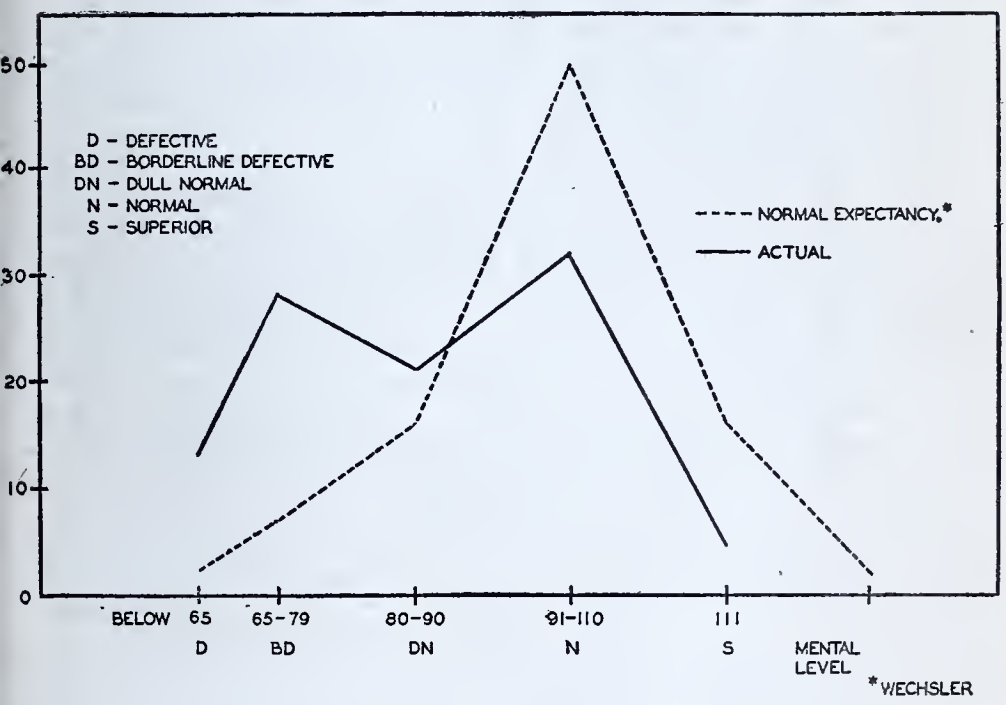
have failed, so penicillin may fail. A rigid criterion of cure in both diseases is indispensable to adequate treatment and control. Pelouze (*7*) has warned that patients who are free from symptoms are not necessarily cured. The public health physician is not entitled to assume cure. He has a medical responsibility to the



community. Even in the practice of mass medicine individualization is indispensable for proper medical care and proper public health safeguards. Considerations should be given also to the possibility that with quicker and less arduous treatments, promiscuity, and consequently venereal disease, may increase.

Stokes (*8*) in speaking about the new weapons for venereal disease treatment states: "That some of the anticipated beneficence may be wishful thinking will almost certainly prove to be the case; for quick and easy cure is turning out as Pelouze has indicated for gonorrhea, to be less of a device for the control of infection

CHART *III.—Normal expectancy and mental level of 553 women appearing before Separate Women's Court February 21—September 22, 1944*



than an incentive to epidemicity through incitement to exposure. Venereal disease dissemination takes place in the period between infection and the institution of treatment control. It is not the patient under treatment who spreads disease but the promiscuous individual before and after treatment. In other words, we must move against promiscuity rather than, or in addition to, disease."

We must, as a matter of necessity, widen our view to include the magnitude and ramifications of our problems in venereal disease control. We must face the expanding front of social factors leading to the dissemination of venereal disease. The social problem of venereal disease knows no geographic nor class boundary lines. The venereal disease control officer must be more than a public health physician. He must coordinate his work intelligently with other agencies. He must do more than treat the sick. He must realize that the avalanche of new venereal disease cases that will continue to descend upon him cannot be controlled by medical treatment alone. Prevention is the health officer's business no matter where it leads him. He has to be a social guide and work on the environment of disease; that is a large part of his business. We must follow the spirochete and gonococcus wherever they go; we have to get the remedy whether medical or social. We cannot do it by just running around with a "luer."

It is necessary as well to get at the root of the social problem

that produces the recruits for new cases of venereal disease. The parent, the church, the school, and the social agency play a vital and important role in an adequately coordinated venereal disease control program, and all of these factors relate back to the kind of a social state the people wish to develop.

Analysis of a great number of new female cases shows the new recruits to venereal disease seldom come from well-organized, tranquil homes; they come from broken homes, homes where the daughter has been left to drift with little parental guidance or assistance. In some instances, the parent has directly contributed to the daughter's delinquency, but in the majority of cases the factors are those of neglect. Therefore, those factors which contribute to juvenile delinquency also contribute to exposure and to the spread of venereal disease.

The church and school must take a more active lead in reaching parents. It is the moral fiber of the Nation, developed by its religious concepts, which has thus far kept venereal disease from becoming more prevalent than it is. This moral fiber must be strengthened in a positive and direct way, because when one deals with promiscuity, one is dealing with conduct and behavior. Venereal disease is only one of the casualties that come from antisocial or irresponsible social behavior. Venereal disease is essentially a problem of youth. This is supported by the fact that the majority of new cases of venereal disease are contracted by boys and girls between the ages of 15 and 25.

Therefore, the parents must be reached and brought to a realization of their obligations in rearing the child in an environment that will build and strengthen a strong moral character. This parent education can be achieved through social and religious education in health and human relations. Such a program is, of course, beyond the scope of any one agency.

To present a military analogy, the program should be defense in depth against venereal disease—in our case, depth in prevention by establishing social standards that will create cultural obstacles to promiscuity, and consequently, to exposure to venereal disease. In cases where these obstacles fail, it is necessary to depend upon medical diagnostic and treatment safeguards. Defense in depth is outlined as follows:

1. Establishment of the family as a secure cultural unit.
2. Achievement of a religious and socially moral outlook with adequate religious training of the child in his moral obligations to his God, his parents, his country, and himself.
3. Establishment of a coordinated health education program in the public schools.
4. Establishment of community recreational facilities.
5. Adequate parental knowledge of child development guidance.
6. Progressive social hygiene instruction of the child by the parent.
7. Continued social guidance to postadolescent youth by the church and State through the recognition of their responsibility to assist the postadolescent to a firmly established, socially balanced, adult life, assisted by trained and adequately staffed social agencies.
8. Recognition on the part of health agencies of their responsi-

bility in guiding the public through health education to recognize the foregoing concepts as indispensable to adequate public health.

9. Adequate social treatment and redirectional care for those who have failed to maintain an accepted social course. This treatment should be made available through community agencies offering assistance in social redirection to the postadolescent through competent and effective service for the individual as a person with a distinct and specific psychic make-up and problem.

10. Active, intelligent, continuous, and diligent repression of commercialized prostitution in its many and devious manifestations and relentless prosecution of the facilitator.

11. Adequate public health education regarding the problems, symptoms, nature, and method of prevention and treatment of venereal diseases.

12. Free diagnosis readily available in the community for all those suspected of having a venereal disease.

13. Adequate and readily available treatment and physical quarantine for those who are unwilling to submit voluntarily to medical care.

14. Free treatment for those who cannot afford to pay for treatment.

15. Active venereal disease case finding and case holding adequately supported by public funds to provide an effective control program by the health department.

16. Recognition on the part of public health workers of the strategic leadership to be given by the health department in building a defense in depth against venereal disease.

The pride of today's medicine is prevention. Treatment for venereal disease may be effective, but the disease and the source of its origin leave scars on the personality and conscience that never heal.

We must always bear in mind the menace of these diseases to the home and to that one divine attribute of man, the power to produce babies—the future of the race. Promiscuity is the worst enemy of the family and the home. Babies diseased at their birth are the greatest of all indictments against any man or woman participating in their creation. The illegitimate boy has been fed into the armies of Europe for centuries. The illegitimate girl without family protection has gone to the bottom of society. Promiscuity will decrease to a marked degree if we can make every boy and girl feel that the greatest happiness on earth can come from honorable marriage and that it is worth while to lead a continent and restrained life.

Our boys and girls need help and knowledge to face this promiscuity that is rotting the family tree at its very roots. There is no family immunity to these diseases.

If the health department takes a negative attitude toward the larger and necessary aspects of venereal disease control or entertains a defeatist or cynical disregard for it, we will fail. If the community is not told the job is more than the medical profession alone can do, we will fail. If the results of promiscuity are to be controlled only through a luer, we will fail. But, if we marshal all the community resources in a united front, and take our place on the headquarters staff with the pastors, the sociologists, the

educators, the peace officers, the prosecutors, and the jurists, we cannot fail.

Nothing less will win the battle against promiscuity and venereal disease.

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The Chairman: Discussion of Dr. Koch's paper will be by the Reverend Father Alphonse Schwitalla, Dean of the St. Louis University School of Medicine.

DISCUSSION

ALPHONSE M. SCHWITALLA, S.J., *Dean,*
St. Louis University Medical School
St. Louis, Mo.

The thought-provoking and challenging paper of Dr. Koch and Dr. Wilbur which we have just heard has many outstanding merits, the greatest of which, I believe, is that it helps us to identify and define one of the central problems in venereal disease control and thus to contribute greatly perhaps to the solution of the problem. Let me juxtapose two questions, both used by the authors of this paper, to bring into bolder relief the differences in viewpoint in the contrasting thinking of two outstanding authorities in our field. Surgeon General Parran is quoted as saying:

"It is my opinion that too often in the past, health officers have neglected their direct medical responsibilities in controlling syphilis and have diluted their efforts by attempting to function in the whole field of social hygiene." I assume that means that a health officer should not be a social hygienist. Is that true? "* * * as a good citizen, the health officer should work wholeheartedly with both. As a public servant, he should do his own job and endeavor to coordinate it intelligently with both."

The authors say: "Even in the practice of mass medicine, individualization is indispensable for proper medical care and proper public health safeguards." And then the authors follow this thought with one formulated by Dr. Stokes, who I believe is also listening to me right now. (Wouldn't it be fine to start a debate between these different people?) The quotation from Dr. Stokes is, "In other words, we must move against promiscuity rather than, or in addition to, disease."

You can see very clearly that there is a very fundamental difference in viewpoint here, and I wish we had time this morning to sharpen these differences, since this is a splendid opportunity for a first-class debate. I am sure that Dr. Parran would roll up his sleeves, and Dr. Stokes is just as ready to roll up his sleeves, and

we could appoint Dr. Koch as the man who keeps the people in their respective corners when the gong sounds.

In our field, is the physician only a medical practitioner or is he more? Dr. Parran would fear that trying to be more he would be less a physician. Stokes believes and so do Koch and Wilbur by implication that being only a physician means for the medical control officer being less than he ought to be.

Dr. Koch and Dr. Wilbur have shown us on the basis of studies of their own which they report, and on the basis of others which they summarize, that there is a relationship between high incidence and occupational migration; between high incidence and occupational stability; between high incidence and social and especially marital stability. They then present to us results of studies to show that there is also an identifiable relationship between high incidence of disease and the more intimate environmental factors and certain social neglects, such as intrafamilial feuds, neglect of school attendance, neglect of church attendance, and absence in the church influence of that subtle but overwhelmingly real factor in church attendance which is to be found in those churches which really regard themselves as the exponents of religion rather than as the exponents of social and recreational programs.

They then pass on to a study of the relationship between high incidence of disease and certain psychologic factors, emphasizing particularly intelligence levels. Now, of course, we can either emphasize in our thinking those facts in that study that would substantiate the thesis that people who have a high intelligence level are not promiscuous, or we can emphasize, if you care to, an abundance of material in the figures submitted by Koch and Wilbur to show that only people who have low intelligence are guilty of any kind of a form of promiscuity. You can canonize the bright people with the high intelligence quotient or you can damn the moron. You have plenty of opportunity of finding material to substantiate either viewpoint in the data that have been submitted.

Sixty-seven percent of the women who appeared before the Separate Women's Court of San Francisco were above the defective and the borderline level. They conclude that while promiscuity as measured between groups of women by the incidence of court cases and by the incidence of infection is to some extent related to low mental intelligence, the evidence is not strikingly conclusive.

Here then is the problem. Assuming that incidence of disease may be used, cautiously to be sure and with proper safeguards, as an indication of, even if not as a measure of promiscuity, how can an attack be made on promiscuity as a cause of venereal disease? The various correlations between incidence of disease and social factors offer relatively little clue. The correlation between incidence of disease and certain psychologic factors also offer little clue. What is left? Can an answer be given?

The total personality of an individual includes more than his intelligence no matter how much importance we wish to attach to intelligence. Character is more than intelligence. Right living demands more than right thinking; self-restraint demands more of a man than restraint of his environment, even more than mere restraint, modification or direction of his mental processes. The

mere availability of remedies offers no assurance of the use of remedies. If we are going to finally conquer venereal disease, we shall have to devise methods for discouraging promiscuity and in the last analysis, what is there left that will restrain a man in a moment of passion except the safeguards of faith in a hereafter, the safeguards of religion. If these safeguards fail, no others can be ultimately effective.

The situation today is more than casually illuminated by the studies of the Social Protection Division. With reference to promiscuity, we are today prepared to accept as valid the differences between "friend," "pick-up," and "prostitute." You remember the investigation was made to determine whether there are behavior patterns, identifiable behavior patterns that can be described, that are different for the friend, the pick-up, and the prostitute. You will also remember, that is, those of you who have been following this literature, that emphasis has been placed on the social behavior, on the intelligence, on the niceties of life, on the places that are frequented by the friend, the pick-up, and the prostitute; we have every reason in the world to accept these differentiations and to attach importance to them. You are touching very closely, as you see, some of the great differentiations between us, and there perhaps you are getting at the heart of the problem to a degree that perhaps no other study has been able thus far to reveal.

Separate behavior patterns in these three categories are recognized. It is recognized, moreover, as is well known and as was brought out again today by Dr. Koch and Dr. Wilbur, the problem of promiscuity today does not focus upon the prostitute. It is recognized that social opportunities have a bearing upon promiscuity. The tavern offers the greatest opportunity for all three types of contact, but the home and hotel are naturally favored by the "friend" and "pick-up." And the most revealing of all is the fact that the automobile can be demonstrated statistically as offering opportunities comparable scarcely to any other for ready availability—and here you are not dealing with the low section of the population.

The lesson of it all is, as I see it, that it is not environment but the character of the persons in that environment who determine whether or not social contacts should culminate in promiscuous acts.

The Advisory Committee on Public Education for the Prevention of Venereal Disease, of which Dr. H. H. Hazen is chairman, has attempted to give a measure of serious consideration to this problem. The question was raised whether the committee should advise the Surgeon General to include comments on the avoidance of promiscuity in the literature on venereal disease prepared under the auspices of the Public Health Service or under the auspices of the several agencies using the advisory facilities of the Public Health Service. The question is a legitimate one for, as was again indicated in Dr. Koch's and Dr. Wilbur's paper, there are those who insist that it is not the function of the medical control officer to exercise other than medical functions. In other words, we must not let the public health agency degenerate into a preaching organization, for fear that when you ask the soldier or sailor or

the civilian to go to the public health department he will say, "I don't want to be preached to or preached at." Is that a legitimate way of looking at things? That was the question which this advisory committee asked itself.

It was hoped that the procedure of calling a conference on this matter might reveal the extent and the intensity of public opinion on the various alternative answers that might be given to the question, and so on April 26 and 27 of this year such a meeting was held. Forty-seven witnesses appeared before the committee or contributed an expression of opinion. The witnesses included officials of many national welfare agencies, editors, or representatives of some of our papers, physicians who more or less represented the viewpoints of groups, health commissioners of some of our cities, welfare workers of various kinds, and representatives of certain governmental bureaus interested in these problems. The purpose was not so much to secure official opinion, but rather to secure public opinion as expressed by representative citizens who by virtue of their position and their personal eminence might be regarded as having secured a measure of competence in this field. Of these 47 witnesses, as many as 35 expressed a definite conviction, in many instances an emphatic conviction, that the publications of the Public Health Service must include warnings against promiscuity if the medical control program is to secure its full effectiveness.

You are not afraid to talk about the etiology of malaria or of pneumonia or of typhoid or of any other disease. Why be afraid to talk about the etiology of venereal disease? The medical man concerns himself with the etiology of all the other diseases. Why should he be afraid to concern himself with the etiology of syphilis and gonorrhea?

Only 3 persons registered an emphatic "no" against this viewpoint, while 9 preferred not to submit a statement on the point. I am not laying stress here upon the statistical results of this study; I am emphasizing rather the growing consciousness that we must more and more approach the individual in the attacks which we are making in safeguarding the Nation against venereal disease. We know that venereal disease can be eradicated if we could put an end to promiscuity. The question may well be raised, will we be able to eradicate venereal disease since presumably we cannot eradicate promiscuity? Medicine can cure venereal disease after it is contracted. Can culture, refinement, love of the decencies of life, idealism, and above all and foremost, true religion, prevent venereal disease by preventing promiscuity?

The Chairman: The final paper before the general session conference is to be presented by Mr. Mark A. McCloskey of the Office of Community War Services of the Federal Security Agency.

VENEREAL DISEASE CONTROL—A WAR ON MANY FRONTS

MARK A. MCCLOSKEY, *Director,*
Office of Community War Services
Federal Security Agency

While I listened yesterday, as a layman and a citizen, to Dr. Heller talk about breaking the chain of infection, I couldn't help but remember that for a long time you people in the medical and health fields have been holding a chain that goes all the way back to Galen and Hippocrates — that you have been disposing of mumbo-jumbo, mystery and magic and bringing people to the point where, during the greatest war in the world, we are free from most epidemics. I think that national public health has paid off well in the catastrophe we are facing.

The Federal Security Agency's Office of Community War Services is one of the arms which has been set up within the Government to meet some of these wartime problems. One of our jobs is the opposite of the thing you have been discussing here—to offer through recreation what our friend from Canada called the substitute activities. Although I am not sure that they are, they do provide some of the things which I care about very much—a decent kind of environment in which our wartime workers and our men in the armed forces can live.

In the Office of Community War Services, we do a job of coordination, too, but I wish I could find a different word for it. The men on our staff have been going into the towns of America to try to put the various pieces we have discussed here together in the form of community organization. Not the least of our responsibility is our part in the fight against syphilis and gonorrhea, and that, rightly, is a job which we do in cooperation with all the other forces lined up against venereal disease.

There are good weapons in this fight. We have the venereal disease educational programs developed by the Army and the Navy, programs which have taught the facts about venereal disease to millions of men in uniform who will return to civilian life. We have the public educational programs of the United States Public Health Service, of State and district health departments, and of private agencies spearheaded by the American Social Hygiene Association. We have systems of reporting and case finding which, through efficient cooperation of military, health, and law enforcement authorities, have uncovered sources and numerous new cases of infection. Daily more infected people come, and will come, under treatment.

The advances on the medical front are phenomenal. We have some intimation that penicillin will play an important part in determining how the future battle lines will form in the march against syphilis and gonorrhea. But no matter how rapid the treatment is, we lose ground unless we find all infected persons, and treat and cure them. It is not yet fully established that the new quick methods of treatment can reduce the prevalence of the venereal diseases to minor proportions within 4 or 5 years after the war, and in the meantime we must address ourselves to the job immediately before us.

All these forces are lined up against the venereal diseases, and they are all essential. Recognition of the need for a cooperative approach in this fight is basic to the program of the Social Protection Division of the Office of Community War Services, the true measure of its effectiveness comes only as it works side by side with all the others against the common enemy.

The social protection program aims to hit venereal disease at the source, by cleaning up its breeding places. This it does through the repression of prostitution and sexual promiscuity and through a redirection and preventive program to help women find ways of life which do not lead to promiscuity or, through the murky trail of the facilitator, to houses of prostitution. Social protection aims to keep the enemy from growing stronger while the medical forces attack him and defeat him.

Through the social protection program, the police have become partners with other community groups in the web of resources tightening around syphilis and gonorrhea. It is their responsibility to control conditions leading to prostitution and promiscuity and to initiate official action against offenders, particularly third parties and procurers. Since 1939, red-light districts have been closed in more than 600 communities in this country. But the holdouts are numerous. Where red-light districts still operate they remain a source of resurgence for the Nation-wide practice of segregation and inspection which could very well come again.

We should be constantly aware that some of the women and girls who were professional prostitutes, before the present drive for law enforcement forced them out of business, are going to return to prostitution. There is no doubt that the promoters of commercialized prostitution believe they can revive their lucrative business when war ends. I suppose that most of them now are dealing in the black markets, but those shabby parasites will be back again wherever there is a loose dollar to be made. For there are human parasites, as well as parasites that live on humans, and in this case they provide the nucleus for the future stock of prostitution. Girls who have operated on their own during the war, whether "for free" or "for hire," are prospective candidates to increase that stock. There is but one conclusion to draw: Prostitution is not dead in this country. It is only dormant. And right there, comes postwar problem Number 1 on the social protection front.

At this point it is well to mention a few of the things for which social protection is striving in connection with its law enforcement work. We will, of course, continue with our two major objectives: First, to drive relentlessly against all persons who profit from the business of commercialized prostitution and, second, to clean up or wipe out the places which contribute to its existence. But in accomplishing these ends, we seek the use of certain police procedures, important in the treatment of sex offenders but equally sound in the treatment of all offenders. We realize that the causes of sex delinquency are, after all, fundamentally the same as those for other kinds of delinquency, and that certain basic principles could very well be practiced by law enforcement officials in handling all cases. These are the procedures we are aiming at in connection with the major objectives which I have just mentioned.

First, we look for greatly increased use of policewomen, for greater understanding in our methods of dealing with prostitutes—who, after all, are not a breed apart but members of the human race. Second, we hold that safe, sanitary, and humane detention should be accorded all arrested persons. Third, we believe that arrangements for medical examination and treatment should be made in all cases of detention. Fourth, we strongly support the policy that juveniles should not be detained in jail unless and until every other possibility has been explored and until every effort has been made to return the child to its home. Fifth, we urge that the court should consider a presentence study of background and other factors bearing on the case and impose sentence on the basis of these findings.

In dealing with commercial factors in the problem, we place insistence on driving out the shoddy aspects of those kinds of businesses which are likely to give facilitators a toehold. The decent cab drivers, saloonkeepers, tourist cabin and hotel proprietors join with us in the effort to expel the shoddy from their ranks. The American Hotel Association, the Association of Taxicab Owners, the Brewing Industries Foundation, the Conference of Alchololic Beverage Industries, and tavern owners associations—all have passed resolutions giving their support to the social protection program. They have not been content with lip service. They have undertaken self-education and self-policing programs which have been of great help in the work of social protection.

Perhaps nothing better exemplifies the close interdependence of the several fronts in this total strategy of attack than the relationship of the police to the health authorities in this control program. These two forces work shoulder to shoulder in the fight against venereal disease. Through the police, numerous cases of syphilis and gonorrhea which otherwise would not be located are called to the attention of medical authorities. It is the policeman's duty to notify the health department when an arrest has been made because of a sex offense. But the police job is to prevent crime and to arrest offenders in contrast to that of the health officer, who locates and treats diseased persons. It is important that this distinction be made clear because too often there has been confusion as to whether the police and the courts were dealing with a criminal problem, a health problem, a behavior problem, or all three.

It cannot be emphasized too strongly that it is no crime to have syphilis or gonorrhea. In a broad sense, however, it is certainly a crime to spread disease, and many States have made the spread—not the having but the spread—of venereal disease a cause for criminal action.

In any event, persons arrested for sex offenses should be charged and tried solely on the basis of offense as defined by law. The business of locating infected persons is ordinarily a public health function and not a police function, except that there are cases in which the health department may call upon the police for help. It is not law enforcement's responsibility to see that the beds in the 63 rapid treatment centers in this country are filled, and they should not be asked to do so. It is true that many of the patients who have been treated in the rapid treatment centers were at one time involved with the police, but their subsequent admission to

the rapid treatment centers was on a voluntary basis.

Even these few highlights indicate the complexity of this business of venereal disease control. It is a battle on many fronts, and no front has the whole answer within itself. Each must work in close harmony with all the others.

Case histories from the rapid treatment centers are another evidence of this complexity. I have never seen one that does not show certain problems of social background that need attention. Patients coming to venereal disease clinics and rapid treatment centers often have social and emotional problems which are related to illness or medical care. Such problems can have far-reaching effects on the future behavior of the patients, and so far, they have not in most cases been handled adequately. Whether the patient goes to a rapid treatment center or to a clinic, she sometimes shows real fear of treatment and fierce resentment or chagrin about her infection. She may have difficulties related to housing, to lack of recreational opportunities, or to the sheer business of earning a living. In addition, if the patient goes to a rapid treatment center, there are problems relating to the care of her children while she receives treatment, arrangements about the living quarters she is leaving and to which she may return, about job interruption, pay checks, rent, clothing, relatives, and so on. And the male patient may have similar problems. They are all typical of the problems which must be handled on the welfare front.

In our economy we can afford to pay for these services. If anything has been made clear in the last 3 or 4 years, it is that we have a productive power in this country which will make it possible to enlarge the kind of work you are engaged in as well as the work of those services which aid you in it—the social service and the welfare service. In any society such as ours, it is obvious that the number of people actually needed to produce food is diminishing and the efforts of increasing numbers of our people can be devoted to bolstering the things we consider fine in human personalities and in community life.

The miracles of medicine, if I may pay tribute to them again, have helped us to define more sharply the relationships of the medical and the welfare fronts in the venereal disease control program. We are much clearer about the procedures through which they should work together now than we were even a short time ago. The reduced periods for treatment of gonorrhea and syphilis make it impossible to provide extensive case-work service at the rapid treatment center and at the clinic. But we do need a skilled worker at the center to whom the patient can turn for guidance on her personal and social difficulties. We need a worker who can provide short contact case-work service, not unlike the intensive service so well developed by Traveler's Aid and some Selective Service boards. Such a worker can refer the individual to the appropriate social agency within the community for whatever continuing service may be needed.

At the clinic, the social and emotional problems of the patient can usually be referred by the medical social worker in the health department to appropriate social agencies in the community. But if there is no medical social worker, clinic personnel should be trained to make effective referrals. Local and private welfare agen-

cies should provide consultation wherever necessary, until this training is complete; but they should not give such assistance with the idea that they are taking over a function which properly belongs to the health department.

The problems which must be handled on the welfare front have their roots deep in the social and economic problems of the past, and they throw some ugly shadows into the future. They cannot be ignored. It took will and courage for the pioneers in this field to undertake venereal disease control as a public responsibility; just so it will take real determination to make the handling of the welfare needs of infected persons a comparable responsibility of government. The redirection aspects of the social protection program are working toward this end.

The Social Protection Division has had a community organization job to do. It has had to identify and define the community-wide problem on the one hand, to take stock of resources to meet the problem on the other, and to focus both views effectively in one clear-cut, community-wide program. It has struggled to coordinate law enforcement, health, welfare, and other services in towns throughout the country. This important task has been accomplished through the organization of community social protection committees with membership representatives not only of law enforcement, health, welfare, and the military services, but also of other vitally interested groups, with the aim of gaining citizen understanding, support, and participation.

This job of coordination is one of the most important contributions made by social protection to the venereal disease control program. It has broken the ground for the kind of all-out community-wide cooperative attack which must be made, if this enemy is to be completely beaten.

Important in the fight against venereal disease is, of course, the moral front. This field is as complex as it is important. While it is primarily the job of the church, the home, and the community, every person must drive on it in his own way. The efforts of any group—medical, political or social—do not assume that social responsibility is a substitute for individual responsibility. Each complements the other and both are equally imperative.

While the moral front is not the immediate responsibility of government, public agencies want to back up the work of the church, the home, and the community, for they are the guardians of this important trust.

There is still one more field of operation which certainly must play an increasingly important role in the future, though it has not been too widely developed so far. If we can look ahead to the peace and visualize the picture as it will be when the military no longer holds its present strategic position in venereal disease control, we will realize that a public opinion front must be opened up to take its place. Public support will be given to this program because venereal disease is esthetically wrong and morally wrong, because it is expensive, and because men everywhere, if they know the facts, will strike out against disease. Military service provided new opportunities for education of millions of Americans in venereal disease control. But this is temporary—and education is a long, slow process. The key to its success is repeated and wide-

spread dissemination of the facts. As the war incentive disappears, the venereal disease control program must enlist continuing and increasing support from the citizens of the country. This it can do through extensive educational programs to drive home in the minds of the American people the seriousness of venereal disease.

We are frequently asked these days, "What will happen to the repression program during the demobilization and postwar period? Will houses of prostitution stay closed after the war and will the Social Protection Division of the Federal Security Agency continue to give national guidance to these phases of the venereal disease control program?"

The question will just about come down to this: Will we take the same measures to prevent the ravages of venereal disease in peacetime that we have taken for war? That question must be answered as all other public questions should be answered in a democracy—by the people themselves.

Certain it is that during the first years of peace, as during the war, the question of venereal disease control cannot be answered without some attention to the law enforcement front as well as to all others. In August of this year, the International Association of Chiefs of Police passed a resolution urging that the repression program be "vigorously supported during the war and thereafter." They took a strong and courageous stand. But after the war law enforcement cannot carry on in the field of social protection as effectively as it does at present unless it continues to receive the national and community support it now has.

Regardless of repression, it is certain that programs for prevention must be stepped up now and in the postwar period. As venereal disease is conquered, the forces which tend to degrade women and to make the higher purposes of sexual life meaningless must also be overcome. As the newer methods of therapy become more readily available to everyone, it becomes increasingly important that we provide opportunities for boys and girls and men and women to meet socially in wholesome environments. Some people fear there will be a wave of sensuality and far-flung promiscuity after the war, because the bars are down and physical dangers have been minimized. Community-wide recreation programs will do much to prevent that kind of demoralization.

I cannot look at the new scientific developments with pessimism. To me progress on the medical front ties in closely with progress on all the other fronts of life. They must all go forward together. Elimination of infection is only part of our job, just as the business of keeping people free from disease in general is only part of the job of the physician. Increasingly, members of the medical profession are taking this farseeing approach to their work.

We do not want our people to be warped in any fashion—morally, physically, emotionally, mentally, sexually. The consummation devoutly to be wished is a full, well-rounded, well-balanced way of life for children and young people and their elders; the end result will be strengthened family life. We should not fear the changes which newer times and newer scientific developments bring. Our only fear should be that we ourselves might become so static that we could not forge ahead with the new and sharper weapons which a generous Providence has bestowed during our lifetime.

As our neighbor from Norway pointed out—and we are neighbors now—disease may be amphibian; it may attack on any front. We can no longer escape the fact, brought home to us by this world melee, that we are coming closer together on this crowded planet all the time. Though it was first said hundreds of years ago, it becomes increasingly apparent that we are tied up together in this whole business of living.

I do not agree that human nature does not change. Even such a basic human relationship as marriage has changed; for until comparatively recent years, it was a business and a biologic fact, without the deep sentiment and the sanctity which now characterize it. When I think of the bestial cruelty of earlier wars and the treatment of people in other ages, I can find reasons to hope this chastisement we are now experiencing will bring some opportunity to realize more fully the potential strength and stature of mankind. I do not believe that the human animal has yet scratched the surface of its own endowments and its own dignity.

As we go forward with you in this whole program—which will make life more interesting, satisfying, and happier—I believe it will have as its base the fact that we cannot violate the personalities of others. With that realization in the hearts of the people, the deep, the true in life will find a greater expression than it does today. It may be that from what we have seen and what we have heard here in the last 3 days we can say for the conquest of venereal disease, "In our time."

The Chairman: Dr. Eugene A. Gillis, Consultant in Venereal Disease Control, New Orleans, will discuss Mr. McCloskey's paper.

DISCUSSION

EUGENE A. GILLIS, *Surgeon*,
United States Public Health Service Consultant, Venereal Disease Control, District Office, New Orleans, La

Prostitution for the time being is no longer a major source of venereal infection. The virtual elimination of red-light districts in most areas represents the cooperative accomplishment of health officers, Federal, State, and municipal law enforcement agencies, the Army and Navy, the American Social Hygiene Association, and the Federal Social Protection Division backed up by an enlightened public opinion. In its role as stimulator and as coordinator, the Social Protection Division has made a significant contribution to this major achievement.

Because of the emphasis which was originally placed on the repression program, many health officers have relied too completely on law enforcement as a substitute for an adequate case-finding program. One hears only too frequently that new cases are not being brought to treatment in a given area "because the police have stopped bringing them in." If this is a representative attitude, it is time to revaluate our case-finding programs. Since prostitution is no longer a major source of venereal infection, it follows logically that police activity will no longer serve as a major epidemiologic weapon.

If you will pardon the quotation of a few figures, I should like

to discuss the case-finding experience of a typical war area in the deep South. This health jurisdiction is adjacent to a large military establishment. It has had an active and vigorous repression program; but it has also developed other case-finding technics.

During the months of August and September 1944, 254 previously undiagnosed patients were found to be venereally infected. An analysis of the reasons for admission in each case reveals that:

85 cases came to the clinic as the result of contact investigation.

16 were supplied by Selective Service reports.

28 came in because routine serologic tests for syphilis had been reported positive.

19 were referred by private physicians.

36 came in voluntarily.

9 were transferred from other clinics.

32 were found through miscellaneous sources.

29 were referred from the jails.

In this instance it will be seen that more than 88 percent of the new cases resulted from sources other than the repression program.

It is not inappropriate to observe in this connection that of these 254 new admissions, 196, or 77 percent, were referred to a nearby rapid treatment center. In this instance, full utilization of the center has freed the clinic staff for an intensified case-finding and diagnostic service.

The foregoing observations might be summarized in this manner:

1. Largely through the activities of the Social Protection Division, prostitution is not at the moment a major source of venereal infection.

2. Health officers therefore must develop a well-rounded epidemiologic program in order to bring infectious cases to treatment.

3. Full utilization of the rapid treatment center frees the clinic staff for a more vigorous case-finding program.

SATURDAY MORNING SESSION

November 11, 1944

The meeting convened at 10:15 o'clock. Dr. J. R. Heller, Jr., presided.

The Chairman: As has been expressed, it is hoped that the recommendations coming out of this conference and the general discussion will lead toward the formation of a newer approach to venereal disease control programs, national, State, and local.

It is realized that the sections have had little time to meet and consider the charges laid down from this desk and for the necessary action in regard to the many points of venereal disease control. It is hoped that these sections, especially the chairmen and secretaries, may continue to serve the Public Health Service as continuing committees. In that way, full advantage can be taken of the opportunities of this conference and the discussion, the viewpoint of those participating in the section discussions, and the substance of the papers delivered here.

However, insofar as possible this morning, we should like to have the full section reports available for the consideration of the conference and for adoption if it meets the approval of the conference.

The first section report is from the chairman of the Section on Diagnostic and Therapeutic Procedures in Gonorrhea, Dr. Rogers Deakin.

REPORT OF SECTION ON DIAGNOSTIC AND THERAPEUTIC PROCEDURES IN GONORRHEA

Chairman: ROGERS DEAKIN, M.D.,
Washington University School of Medicine
President, American Neisserian Medical Society
St. Louis, Mo.

Secretary: C. J. VAN SLYKE, Senior Surgeon,
Assistant Chief, Venereal Disease Division
United States Public Health Service, Washington, D. C.

Dr. Rogers Deakin: I am sure that all of you regret, as I do, the absence of Dr. Oscar F. Cox, secretary of the American Neisserian Medical Society who had been designated as the chairman of this Section. He became ill shortly before the meeting was to take place, and I apologize for my deficiencies as chairman pro tem.

I should like to express my appreciation to the individuals who participated in our Section program yesterday afternoon. Some of these men received assignments to discuss various phases of gonorrhea at a very late date, and it must have been quite a chore to prepare these reports within such a short time. Nevertheless, I am sure that those of you who attended the Section meeting felt that the reports were extremely worth while, interesting, authoritative, and well-considered. I hope their publication at some future date will be authorized, so that all of us will have an opportunity to read them in more detail.

I should like to express deep thanks to those who attended the Section meeting and participated in a very lively discussion after the program. I hope it did not last too long. The room was crowded, hot and smoky; nevertheless everyone seemed to have a good time.

I should like also to express my very deep appreciation to our energetic and hard-working secretary, Dr. Van Slyke.

The Section on Diagnostic and Therapeutic Procedures in Gonorrhea has considered the problems bearing on the postwar control of gonococcic infections and has the honor to submit the following comments and recommendations:

The diagnosis of gonorrhea is made either on a presumptive basis or on an absolute basis. In the absence of cultural confirmation, a presumptive diagnosis of gonorrhea is made on spread, epidemiologic, and/or clinical evidence of the disease.

It has seemed to us that represented something which you and I recognized, and the fact that we really have to make a presumptive diagnosis—and we have attempted in one sentence to express just that fact—that it may revolve around spreads, it may on occasion revolve around epidemiologic data, and, of course, we cannot ever disregard the clinical manifestations of the disease.

An absolute diagnosis is based on the detection and isolation of the gonococcus, confirmed by carbohydrate fermentation tests together with acceptable clinical evidence of the disease.

The Section recommends that wherever it is possible laboratory facilities of high quality be made readily available to health departments and the medical profession in order that laboratory procedures may be brought to bear on the diagnosis. The Section recognizes the practical limitations affecting the fulfillment of a complete laboratory program. The reporting of the presence of Neisseria gonorrhoeae based entirely on the finding of so-called typical colonies which are oxidase positive is condemned by this Section. This practice is somewhat less objectionable if, by spread examinations, the organisms of the colony are shown to be gram-negative diplococci morphologically resembling the gonococcus.

Present evidence indicates that the early promise of sulfonamide compounds in the therapy of gonococcic infections has not been fulfilled.

I think all of us regret that that statement has to be made, and I believe that at the same time we feel we would not be accurate if we did not make the statement.

On the other hand, the recent introduction of penicillin into the field of therapy for gonococcic infections appears to offer an extremely important step toward the control of these infections, in that penicillin is highly effective, rapid in its action, and without significant toxic effects. At present, it cannot be said that the time-dosage relationships governing the administration of penicillin in gonococcic infections have been firmly established. It was the consensus of the Section that present dosage schedules have been somewhat influenced by the current scarcity of penicillin. The Section recognizes the limitations imposed by the present curtailed supply of penicillin and urges that the present trend toward employing penicillin in minimal to moderate amounts be supplanted by a turn toward a more generous administration of this valuable compound, when increased supplies make this dosage possible.

I should like to interpose this statement at this time. You already realize that we have been quite general in the statements. We have not felt that we could be too specific. Dr. Heller, we tried to answer your questions as you proposed them in your opening

remarks, but I think it was the consensus of the Section that many of the questions cannot be given definite answers at this time. If we are too general in our remarks in our report, perhaps a further discussion will help to delimit these observations and remarks.

The very recent and preliminary studies on agents such as beeswax and peanut oil, which inhibit the absorption of penicillin deposited intramuscularly offer prospects of substantially curtailing the period of treatment. The Section recognizes the value of this approach and urges that studies of this type be encouraged.

Pending widespread availability of penicillin—the therapy of choice—the Section favors continuation of the use of the sulfonamide drugs according to previously accepted dosage schedules, and the use of conventional types of local treatment or fever therapy for those who have sulfonamide resistant gonorrhea.

To qualify or repeat that statement: "The Section favors continuation of the use of the sulfonamide drugs according to previously accepted dosage schedules, and the use of conventional types of local treatment or fever therapy for those who have sulfonamide resistant gonorrhea, where penicillin is not available."

The Section finds that the incidence of complications seems to be on the decrease. The complications of gonorrhea appear amenable to penicillin therapy. It is often necessary, however, to employ larger doses over a longer period of time as compared to the time-dosage schedule in the uncomplicated infection. For certain complications, it may be necessary to employ adjuvant therapy, such as immobilizing casts for the more destructive lesions of arthritis.

I am sure it was not the feeling of the Section that the gynecologist, the orthopedist, the ophthalmologist, or the urologist should be pushed out of the picture. It seems to me, personally, quite obvious that there will be, on occasion, individuals in whom present-day chemotherapy has not been entirely successful, where the knowledge and services of men who are dealing with female diseases, preferably urinary diseases, heart conditions, or orthopedic conditions will be called for.

In the limited number of cases which do not respond satisfactorily to penicillin therapy, in that the disfiguring or disabling effects of the complications persist, surgical treatment may be required.

The Section considered the criteria of cure of gonococcic infections. The presentations of the discussants clearly demonstrated that the higher the quality of culture investigations the less confusion arose as to the determination of cure. The failure to perform, or properly to perform, differential carbohydrate fermentation tests, has led to the detection and designation of certain nonpathogenic organisms as gonococci which are not amenable to penicillin therapy.

It was stressed that a single negative culture following penicillin therapy was not, with very rare exceptions, succeeded by cultures which later demonstrated that the patient continued to harbor the gonococcus. The Section urges that repeated culture studies concerned with tests of cure be undertaken where feasible, but recognizes and recommends that a single negative culture following penicillin therapy be accepted as a practical measure in determination of cure.

The Section is cognizant of the limited experience available on which a final proof of cure following penicillin therapy is based, and proposes that the results of more extensive and more prolonged investigations of the efficacy of penicillin be the basis for qualifying its recommendations, either towards greater stringency or to the elimination of cultural requirements, as regards proofs of cure.

Separate from but entirely related to the criteria of cure the Section recognizes the possibility of a syphilitic infection being acquired concomitantly with the gonococcic infection. The Section therefore recommends: (1) That each gonorrhea patient be properly informed as to this possibility; (2) that the subcurative influence of the amount of penicillin given for the gonococcic infection to alter or to mask effectually the early symptoms of syphilis be strongly impressed upon the patient by verbal and printed warnings; (3) that the patient be reexamined whenever untoward signs or symptoms occur, and (4) that a serologic blood examination for the detection of syphilis and a physical examination be made approximately 2 months posttreatment.

The diagnostic significance of the satellite bubo is stressed as well as the interfering action of even small amounts of penicillin on the results of darkfield examinations.

The Section is not in possession of information concerning new or improved methods of prophylaxis. The development of a stable and highly effective chemical prophylactic agent which can be applied repeatedly without irritation and which is acceptable in that it is not messy and is readily employed would be a valuable contribution. The cooperation of the armed forces in conducting large-scale field trials of such likely compounds as may be presented is invited.

The possibility of prophylaxis through the medium of immunizing against gonorrhea was discussed. The difficulties of preparing and testing the fraction or fractions of the gonococcus which may have antigenic properties and be capable of producing a suitable degree of immunity were recognized. Because of the complexity of the special problems involved, further considerations of this possibility were delegated to certain members of the Section and are not here the subject of recommendation by the Section.

The Section recommends that extensive research activities be conducted. Experimental investigation is required to develop further the knowledge concerning the biology of the gonococcus and as related to the possible role of effecting immunization procedures. There must be a continuing effort to improve the media employed in the cultural diagnosis. The whole field of therapy must be constantly under review, and at present, emphasis should be placed on determining the role of penicillin absorption inhibitors in the therapy of gonorrhea.

The Section recommends the close coordination of the health officer and the physician in private practice in order that all patients with gonococcic infection can be brought to treatment as quickly as possible.

This concludes the report, as those who collaborated with us in trying to condense what was said yesterday afternoon were able to do it.

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There is one thing I should like to add. It must be recognized that with penicillin we do not have an opportunity to pursue the clinical cooperative studies which have been possible when the sulfonamides were used, and no one understands any clearer than I the war needs which made that impossible; nevertheless, I think I am justified and may be permitted to hope that when there is an opportunity for an extensive clinical cooperative investigation involving civilian agents, as well as military agents, that some such effort will be initiated.

Dr. Deakin: The Chairman has suggested that I move the adoption of this report. I do so move.

The Chairman: It has been moved that this report be adopted by the conference. Do I hear a second?

Dr. P. S. Pelouze (Philadelphia, Pa.): I second the motion.

The Chairman: Dr. Pelouze seconds the motion. It is now open for discussion.

Dr. Udo J. Wile: There is one recommendation in this report that I would like to see amended, and that has to do with the use of penicillin in patients who have contracted gonorrhea and syphilis at the same time. Under unusual conditions, the chancre of syphilis may be delayed as long as 90 days. It is to be assumed that when penicillin is given for gonorrhea in a patient who may be in the period of primary incubation for syphilis, the progress of this infection may be retarded much longer than 2 months. It would seem to me that it would be wiser to recommend that patients who have been so treated have a physical examination and a blood test at the end of 2 and 3 months' time.

The Chairman: Is there discussion on Dr. Wile's suggested amendment to the report? If not, Dr. Wile, will you put that in the form of an amendment so that the house will understand it?

Dr. Wile: I would, therefore, move to amend the suggestion or the proposal that was made in this report, that in patients who have been treated for gonorrhea, examinations for coexisting syphilis be made at the expiration of 2 and 3 months' time.

The Chairman: You have heard the amendment. Do I hear a second?

Dr. Pelouze: I second the motion.

The Chairman: It has been moved and seconded. Questions? Those in favor please say "aye." Opposed. The "ayes" have it and it is so ordered. Is there additional discussion of Dr. Deakin's report of the Section on Diagnostic and Therapeutic Procedures in Gonorrhea?

Dr. H. G. Irvine (Minneapolis, Minn.): It is not clear to me whether a single culture should be accepted as part of the criteria of cure of gonorrhea. I do not recall that a time element was given as to how long after completion of treatment the single culture should be taken.

The Chairman: Dr. Deakin, would you answer the question regarding the time relationship of the culture?

Dr. Deakin: I do not believe that was specified in the report. I think the impression was that it be done within 24 hours after completion of treatment.

Dr. Irvine: I think it is of great importance because gonococci may be temporarily dead and the culture may not show anything; yet, there may be enough gonococci to revive the situation in a week or 10 days when the culture might show something.

The Chairman: Is there additional discussion on the point involved as to the time these cultures should be taken after therapy?

Dr. C. J. Van Slyke (Washington, D. C.): I should like to comment, in answer to Dr. Irvine's question, that our experience where we have had men and women under control in prisons, and the experience reported to the Section by men who run the rapid treatment centers is to the effect that a single negative culture obtained 24 hours after treatment is practically never followed by a subsequent positive culture. Dr. Robert D. Wright, of the Kanawha Valley Medical Center, reported one instance among approximately 500 patients.

I think that theoretically there is some objection to taking the culture 24 hours after treatment because of the effect of penicillin in inhibiting the growth of the gonococcus on the culture plate. I can but feel, however, that

the effect of the penicillin on culture media, which are, unfortunately, not quite as sensitive as we would like to have them, is more of an academic than a practical problem.

May I put it this way: In many, or possibly in most, of the rapid treatment centers and in most clinic patients or those at the clinic level, the incidence of new cases of gonorrhea in the group which has been discharged, the incidence of new infections developing, will be considerably less than the occasional case which may be missed by not taking cultures at a later period or taking more cultures. I think that the practical considerations outweigh the theoretical conditions in this instance.

The Chairman: Is there additional discussion of this or other points?

Dr. H. P. Talbot (State Department of Health, Conn.): I should like to raise a question with regard to what we State health officers are going to recommend as to cultures when we return home. I realize that the committee did not make comment as to culture media for transporting specimens to laboratories. I think the omission of that is to be looked down upon. We who are going back to our States to recommend to physicians something practical must give them something practical. I wish that they would study further as to what can be done in arousing the interest of physicians for, after all, they are the ones with whom we must work to clear up the problem of gonorrheal infection.

The Chairman: It may be recalled that many problems cannot be met wholly at this conference and it is realized that there must be further study of many of these points. It seems to me that the problem just discussed is a good one for the additional consideration of this committee. Is there discussion on this point?

If there is no additional discussion on the report, we are ready for the question. Is it the will of the conference that this report be adopted by the conference as the recommendation of the Section on Diagnostic and Therapeutic Procedures in Gonorrhea? All those in favor please say "aye"; opposed. The "ayes" have it.

The Chairman: The second report before the conference is that from the Section on Diagnostic and Therapeutic Procedures in Syphilis. The Chairman is Dr. A. W. Neilson.

REPORT OF SECTION ON DIAGNOSTIC AND THERAPEUTIC PROCEDURES IN SYPHILIS

Chairman: A. W. NEILSON, M.D.,
Consultant, Midwestern Medical Center
St. Louis, Mo.

Secretary: HOWARD P. STEIGER
Passed Assistant Surgeon (R)
United States Public Health Service
Charlotte, N. C.

Dr. A. W. Neilson: I wish to thank all those who participated in the Section meeting yesterday afternoon.

I must apologize to the men who were not notified until the last minute that they were to be participants. Sickness and the pressure of some other important matter often made it impossible for scheduled speakers to arrive; others were asked to fill their places and did so admirably.

I wish to thank Dr. Howard Steiger for his invaluable assistance both as Secretary of this Section and as coauthor of this report.

I am almost afraid to read this report because of the tremendous mass of material that was covered. It was an extremely difficult problem to wade through the data and to extract from it those things that were most important, and to leave others unmentioned.

Needless to say, somebody's toe is going to be tramped on; needless to say, we are going to be criticized. However, here it is.

Two days ago, from this same platform, Medical Director J. R. Heller, Jr., Chief of the Venereal Disease Division, United States Public Health Service, charged the Section on Diagnosis and Treatment of Syphilis with certain responsibilities. This conference during the last 2 days has attempted to evaluate and search into the many problems growing out of the newer treatments of syphilis. Many different types of treatment of syphilis have been discussed, and arguments both for and against their use have been propounded. A great deal of scientific data has been given us, and dozens of charts, graphs, and statistical tabulations have been analyzed.

All of this has been done with the point in view of attempting to answer Dr. Heller's charge.

In planning this sectional program, we kept in mind the necessity of including, to the best of our ability, those men whose work has established them as leaders in their respective fields of investigation. The meeting was subdivided as follows:

1. Penicillin.
2. Intensive arseno and fever therapy.
3. Diagnosis.
4. The management of syphilis in the Services.

Let us consider the first of these categories, penicillin; again we divided this into types of syphilis. For early syphilis the following recommendations were made:

1. 1.2 million units of penicillin in 7½ days will be continued, since sufficient information has not been accumulated to adequately evaluate this schedule.

2. 2.4 million units of penicillin in 7½ days will be continued by the Army and Navy, and there is no need for civilian investigation of this method.

This is true because obviously there are sufficient cases that will be run by the Army and Navy.

3. 1.2 million units of penicillin in 7½ days, plus daily injections of 40 mg. mapharsen. It is estimated that the mortality by this method will be approximately 1 in 5,000 cases.

4. 1.2 million units of penicillin in 7½ days, plus 1 gm. bismuth subsalicylate given in 5 injections concurrently.

5. 1.2 million units of penicillin in 7½ days plus fever.

Late syphilis: Penicillin is effective in a considerable proportion of late syphilitic manifestations.

1. Penicillin has little or no effect on reversing fixed positive blood serologic reactions.

2. Penicillin has an arsenic-like effect and will probably replace arsenic, particularly the pentavalent arsenicals.

3. Penicillin has a striking effect in grade I and grade II spinal fluids, and its efficacy in grade III spinal fluids is inversely proportional to the duration and extent of the infection.

4. Treatment of grade III spinal fluids with 2.4 million units of penicillin in 7½ days is justifiable. Initial doses should be reduced to prevent reactions.

5. The effect of penicillin plus fever in late syphilis has not been determined.

6. Treatment resistant central nervous system cases sometimes respond to penicillin.

7. Preliminary evidence indicates that early cases of tabes and paresis are clinically improved by penicillin therapy.

8. Preliminary evidence indicates that penicillin is effective in acute syphilitic meningitis.

Congenital syphilis: 1. The results in syphilis of the newborn are comparable with those of early acquired syphilis.

2. Preliminary evidence indicates that the effect of penicillin in juvenile neurosyphilis is good.

3. Penicillin has erratic and difficult interpretable effect in the treatment of acute interstitial keratitis and may have deleterious effect.

I spoke to Dr. Stokes just before the meeting about this point, and he felt that a word of warning should be interjected. Penicillin is not without its reactions. One is always very careful when he treats interstitial keratitis with anything. We wish to caution in the use of penicillin in interstitial keratitis.

The treatment of syphilis in the newborn should begin immediately upon the establishment of the diagnosis, and one should not delay until the nutritional status of the child is optimum. Initial doses should be low and treatment should continue over a long period.

Penicillin therapy by slow absorption: 1. Single daily injections of 300,000 units of penicillin in beeswax and peanut oil, over a period of 8 days, have maintained constant levels of penicillin in the blood.

2. Disappearance time of spirochete from lesions is less than 12 hours.

3. Single large doses of penicillin in beeswax and peanut oil do not cause abnormal reactions.

4. Immediate posttreatment quantitative serologic trends are similar to the pattern observed in penicillin in saline.

5. An ambulatory method for the treatment of syphilis with penicillin may be available.

6. It is interesting to speculate whether or not a single large dose of penicillin in a suitable menstruum would abort a coexistent syphilitic infection in patients with early acute gonorrhea.

The following motion was unanimously adopted by the Syphilis Section:

That the cooperative study of penicillin in early and late syphilis under the general auspices of the Committee on Scientific Research and Development, in participation with the United States Army, Navy, and Public Health Service, be continued for a period of 5 years from now, or until adequate data have been obtained as to optimum methods or doses. Further, when the total demobilization of the armed forces occurs at the cessation of hostilities, and the financial support of these studies thereafter ceases, the cost of the continuation of this program should be assumed by another organization, governmental or otherwise.

Intensive arseno and fever therapy: 1. Intensive arsenotherapy is a wartime expedient for the control of infectious syphilis and is not recommended for use outside a hospital by inexperienced personnel.

2. The cure rate is about the same as that of completed conventional therapy and has the advantage of reaching the individual who would not complete routine therapy.

3. More reactions are to be expected from intensive therapy than from routine therapy.

4. Since an estimated 60 percent of all patients started on routine therapy do not receive enough treatment to prevent relapse and late sequellae, intensive therapy is justified, provided the incidence of reaction is kept at a low level.

5. According to competent observers, fever therapy alone will not cure early syphilis.

6. Fever doubles the toxicity but quadruples the efficacy.

7. The incidence of satisfactory results with combined fever and arsenotherapy compares favorably with intensive arsenotherapy.

Diagnosis: 1. The establishment of a diagnosis of syphilis by darkfield examination should be acceptable only when done by trained personnel and subject to final interpretation in the light of clinical findings.

2. False positive reactions due to nonspecific causes and technical errors are relatively common. Repeated physical and serologic examinations are indicated before treatment is instituted.

3. It is conceivable that false positive and fixed positive reactions occur in the spinal fluid as well as in the blood.

4. Epidemiologic efforts must be intensified to keep pace with accelerated treatment programs since an increased number of reinfections may be expected.

5. Although a great deal of scientific investigation is in process at present, no satisfactory test has been evolved for the conclusive differentiation between the false and the true syphilitic positive reaction.

Armed Forces: The treatment of early infectious syphilis with 2,400,000 units of penicillin in 7½ days is the method of therapy accepted by the Army and Navy at present.

Dr. Neilson: The foregoing is respectfully submitted by the Section on Diagnostic and Therapeutic Procedures in Syphilis, and I move that it be adopted by this conference.

The Chairman: The adoption of this recommendation by the conference has been moved. Do I hear a second?

Dr. Udo Wile: I second the motion.

The Chairman: The recommendation is now open for discussion.

Dr. Stokes: Dr. Neilson was so unwise as to mention my having been consulted about some aspects of this matter, and I have to rise to the occasion. The problem of presenting a report on a matter like this is a desperate proposition to confront any man, and I think the men who tackled this job should receive citations of merit of some sort from the Public Health Service.

I saw the report rather late this morning, and there are some suggestions, essentially minor perhaps, that, since I did have an opportunity to see the report and to think it over a little, I should like to put up for consideration. I do not think I will stand back of them as amendments without considerable discussion from the floor, but I would venture to name them.

Since I was the spokesman for late syphilis in the general summation, I will start with that.

Penicillin is effective in a considerable proportion of late syphilitic manifestations. Since it has been elaborated upon quite extensively, would it not be possible to insert "benign syphilitic manifestations" and make that a special case under 4?

"Treatment of grade III spinal fluids with 2.4 million units of penicillin in 7½ days is justifiable." I should like to see the high dosage schedule fully

recognized here, and to see 2,400,000 to 4,000,000 used instead of simply 2,400,000.

Under the item of "Penicillin therapy by slow absorption," I have this feeling: In comparison with the amount of energy and organization which has been devoted to the use of aqueous solutions of penicillin intramuscularly, the amount of work done on penicillin in oil suspension, even by able and competent investigators, is infinitesimal. Therefore, it seems to me that it is a little premature for a national gathering to make recommendations on the use of penicillin in oil suspension for the treatment of syphilis; perhaps I am wrong about that, but national conventions have great weight. We like to feel that physicians all over the country can look at this document and proceed to use practically the recommendations we have made.

I certainly, although I have worked some with penicillin in oil and I know Captain Romansky appreciates the extreme complexities of the problems for he told me so, would not be willing to recommend to practitioners at large over the country, or even to experts, that they begin the treatment of syphilis now with penicillin in oil. I would, therefore, suggest that in place of this careful and factually correct statement regarding penicillin in oil, we substitute the statement, "Penicillin by absorption-retarding methods, such as oil suspension, is under investigation and shows promise."

I have one or two other suggestions on the report under "Diagnosis." You see the statement, "False positive reactions due to nonspecific causes and technical errors are relatively common." I have had the misfortune to be one of the responsible investigators on an OSRD contract, studying the biologic false positives for the past year. I may say that there is no meaner problem at present facing syphilologists than this particular one, and it is certain that many people are carrying heavy loads of bismuth in the back pockets who would much better be carrying the cash that they represent, so far as their physical welfare is concerned. There is no question of that. On the other hand, as syphilologists, we have recognized for many years the great danger of discrediting what little we do know about how to find out whether a person has syphilis or not. I think we are now on the swing of the pendulum in which a motion to discredit would be rather willingly received by many persons. Accordingly, I think great caution must be exercised in phrasing any statement which takes the edge off the diagnosis of syphilis or tends to take it off.

Some very curious things are happening, it appears to me, now that I am reaching the spectorial phase of my career as distinguished from the active phase, in the management of venereal disease. I did not rise—I have a constitutional timidity as you know—to discuss this suggestion that nothing but observation be applied to dealing with the patient who has gonorrhea masking a syphilitic infection which we have not yet recognized. Perhaps you remember years ago the violence of the discussion, similar in strain, over the question of identifying syphilis in the presence of chancroid in time to do something mandatory and energetic about the syphilitic infection. It reached polemic proportions on the other side of the water, and there was a strong school which insisted that clinical chancroid should be treated as syphilis. Now the question arises as to whether clinical gonorrhea should be treated as syphilis, if, as much experience tends to indicate, 20 percent of the syphilis may be masked by gonorrheal infection and escape recognition altogether.

This situation is becoming acute, because a 300,000-unit dose of penicillin and 350 or 320 milligrams of mapharsen look so good in the cure of syphilis, it is a question whether they ought to have recognition in a situation of this sort.

I have been, of course, as all of us have been, beset by questions from physicians confronted with this problem of what to do about coexistent gonorrhea and unrecognized syphilis. I have gone all out, with my neck and arms extended, to say that there is strong reason to suspect that a patient has both infections, if he acquires his gonorrhea under circumstances and in an area, shall we say, where a very high syphilis rate is coexistent. It might not be unreasonable in the armed forces to consider giving him 300,000 units of penicillin and for good measure adding 320 milligrams of mapharsen; then we have done a lot about his masked early and probably 100 percent or 99 percent curable syphilis.

Now, returning to this question of the diagnosis of syphilis, is it entirely wise to overstress the frequency of biologic false positives? "Relatively

common," is that vigorous term to use of a biologic false positive as at present understood. It is a wave phenomenon, apparently, that has rather intimate connection with waves of epiglottic infection and of respiratory types, for example, and there are parts of the country and times of the year when biologic false positives may be perhaps more common than at others, but it is by no means an overwhelming phenomenon as yet which compels the abandonment of our previous ideas with regard to the worth of serology in the diagnosis of the disease. Therefore I would say something like: "Technical errors and nonspecific causes are recognized," or are not uncommon, or something a little less strenuous than "relatively common," which is certainly a black eye for serologic tests of syphilis. It still has one eye to see out of, but the other is gone after a statement like that, it would seem to me.

Then this sentence, "Repeated physical and serologic examinations are indicated before treatment is instituted." We are approaching the day, may I speculate, when a civilian who thinks he has been exposed to syphilis will treat himself for the disease in advance of its manifestation, so agreeable and so inexpensive will the treatment be. So that we should not do anything to discourage by overtechnical and exacting requirements the prompt, energetic treatment of early syphilis. I, therefore, suggested a rephrasing to myself. "It is recommended that the confirmation of serologic tests when essential to diagnosis be practiced." I cannot see any reason for taking 2 or 3 Wassermann tests on a person who has a positive dark field, with fairly competent help available, although I understand that very early in this conflict that was a not uncommon practice. "That physical examination be regularly employed, but that the early diagnosis of seronegative and seropositive primary syphilis be not endangered by undue skepticism on the efficacy of diagnostic tests." Just a little more culture in the phrasing of that statement, it seems to me, would be in order from a body whose statements will have the weight and seriousness that we hope we shall have.

The Chairman: We would like discussion on the points raised by Dr. Stokes in his compilation of this paper. Dr. Moore, have you any discussion?

[There was no discussion.]

The Chairman: Your Chairman was unable to get the points in the order as given by Dr. Stokes. As I recall them, some would probably merit considerable discussion by the conference, unless there is agreement that they should be incorporated in the report. It would seem that probably they could be made in the form of a general amendment to the report, if agreeable to the conference, rather than taking them up point by point. Is there disagreement with the points mentioned by Dr. Stokes or are they concurred in?

Dr. Irvine: Mr. Chairman, may I make one suggestion relative to the diagnosis on the basis of serologic findings, which might not only be of help so far as the diagnosis is concerned, but which, I am convinced, will also help to settle the situation, to a degree at least, as to the false positive.

We have had perhaps a unique experience in Minnesota inasmuch as every questionable first test for the Selective Service has been followed by a second test with a complete battery of not less than 7 tests. I think our experience proves without much question that frequently persistent 4 plus tests may be found with certain tests only, and that when we say that the diagnosis should be based only upon repeated tests, in a great many States and places that will be confined to certain individual tests. I say this with all due respect to the originators of the individual tests, but our experience demonstrates, I think beyond question, that we may have certain tests show positive repeatedly in serums, when several other tests are completely negative. I should like to suggest that we add not only repeated tests, but a variety of additional tests in every specimen before diagnosis is made.

The Chairman: Is there discussion of Dr. Irvine's point advocating a battery of tests rather than reliance on one?

Major Charles R. Rein[1] (Medical Corps, Army of the United States, Washington, D. C.): I should like to disagree with the use of a battery of tests. There is an old saying in serology that if you do one test you have one headache; if you do 7 tests you will have 7 headaches to worry about. I think the Army has taken the right course in this type of thing. I believe we all agree that false positive tests do occur. I agree with Dr. Stokes that we are probably emphasizing this condition too much, that certain physicians will take advantage of the fact that this conference recognizes that false positive blood tests occur rather frequently, and will dismiss patients as being false positive because they happen to like the patients or they come

[1] Now Lieutenant Colonel.

from the proper social status.

These false positives do occur and they should be watched for, but the course that the Army has taken has been very fruitful. The majority of the false positive blood tests occurring now are the type that follow acute infections of some type, usually upper respiratory infections, but the large majority of them revert to negative in 2 or 3 weeks or a maximum of 3 months. If a physician has a positive blood test, uncorroborated by history or physical findings, there is certainly no harm in watching that test by repeated titers. If the particular patient does happen to have latent syphilis, no harm has been done by watching the patient and withholding treatment for a period of 1 or 2 months. We do that in the Army all the time.

If a patient is treated for syphilis on the basis of uncorroborated serology, and after 2 or 3 injections the physician decides it was a false positive, that patient is a dead pigeon; once you treat a patient for syphilis he has it, and because the blood becomes negative, you will never know whether it became negative due to treatment. Uncorroborated serologic reactions should be watched for a short period, and a 3-month period is too long.

The Chairman: Is there additional discussion?

Dr. C. G. Baker (Lexington, Ky.): From the standpoint of diagnosis, caution should be used in the recommendations of this body which go out to private physicians and others who may not be specialists in treating syphilis. I think they should be cautioned. In other words, where a darkfield examination is negative and the blood test becomes positive, and there is delayed reaction, that is as important as a false positive test, or possibly more so. As a matter of caution, those tests should be repeated sufficiently to rule out the fact that a positive test may develop later.

Dr. Moore: Not to change the subject too abruptly from beeswax to battleships, but it is not quite clear in my mind as to whether some of the comments made by Dr. Stokes with regard to the possible desirability of treating patients with gonorrhea without any evidence of syphilis are to be incorporated in the recommendations of this group.

Dr. Stokes: I made no such proposal.

Dr. Moore: If Dr. Stokes' remarks might have been interpreted in such a manner as to indicate that under special circumstances when a patient acquires gonorrhea in an area where the incidence of syphilis is high, the abortive effect of treatment for syphilis might be a highly desirable thing to employ—then, with that point in view and with due consideration of the possible effect of penicillin in masking the development of early syphilis, I should like to disagree. I think it would be highly undesirable to treat patients who have gonorrhea as if they had syphilis, since in our experience in an area in which both diseases are extremely prevalent, the acquisition of syphilis with the acquisition of gonorrhea is an extremely rare phenomenon, certainly not in the neighborhood of 20 percent but much more likely in the neighborhood of 1 percent or less. In most of those patients not penicillin-treated, we do not see masked early syphilis; we see simultaneous early syphilis, but not masked early syphilis. I hope, therefore, that the panel will not incorporate in its recommendations a suggestion that we kill two birds with one stone when one of those birds may not yet even have been born.

The Chairman: Dr. Stokes, I wonder if you would be kind enough to recapitulate briefly those points. Your Chairman admits laxity in taking them down properly, and I think it might be desirable to present them to the audience for contemplation and, if possible, incorporation as an amendment.

Dr. Stokes: I was making no recommendation to the committee responsible for recommendations on gonorrhea, and I am sure you all realized that. I was just dreamily philosophizing about the queer things that seem to impend in venereal disease control, some of which have already been realized.

The first suggestion I made was with reference to the incorporation of penicillin therapy by slow absorption. I suggested that instead of detailing the procedure, which has been reported as an investigative matter, we simply say that penicillin by absorption regarding methods, such as suspension in oil, is under investigation and shows promise. I would hate to see that method made popular at this particular time, much as I think it may be the method of the future. That was my first suggestion.

As to the second one, I suggested a rewording of the second sentence in item 2, instead of "Repeated physical and serologic examinations are indicated before treatment is instituted." I also suggested that in place of "relatively

common," after "false positive" I would like to see the word "serologic" inserted—"False positive serologic reactions due to nonspecific causes and technical errors are relatively common." I would like to see a phrase like "not uncommon" or "are matters of interpretative importance," instead of a statement using "common" or "uncommon."

Then, the next sentence I would reword to read, "It is recommended that the confirmation of serologic tests when essential to diagnosis be practiced." A patient with a primary lesion and a positive Wassermann reaction and a dark field which is positive by reasonable competence in examination, does not require 2 or 3 Wassermann tests before it is accepted that he has the disease. Now and then somebody is going to get by with a chancroid or something of that sort, but there are not going to be enough to justify weakening the test.

"That physical examination be regularly employed." Perhaps you would prefer "routinely employed," but that the early diagnosis of seronegative and seropositive primary syphilis be not endangered by undue skepticism of the efficacy of diagnostic test.

I think that summarizes my suggestions, but I have one or two minor words. I suggested that the statement "Penicillin is effective in a considerable proportion of late syphilitic manifestations" be changed to read "benign late syphilitic manifestations," but I see by the way this is subdivided here that is a general statement regarding penicillin rather than one to be limited by a single word. I believe that concludes all I have to suggest.

The Chairman: Is there additional discussion of the points brought out by Dr. Stokes as a possible minor amendment of the report? If not, I should like a motion as to the incorporation of the sense of this amendment of the report. Do I hear a motion to that effect?

Dr. Talbot: I so move.

The Chairman: It is moved and seconded that these suggestions by Dr. Stokes, that is, the sense of the suggestions, be worked out along the lines that he mentioned, and be incorporated in the report. All those in favor please say "aye"; opposed. Carried.

We would like additional discussion of the report from the Section.

Dr. D. W. Goldstein (Fort Smith, Ark.): When we get home, we will be asked by general practitioners what is recommended to them. The recommendations in this report are only for hospital treatment, as I understand them. In the report on gonorrhea, it was stated that for the present the sulfonamide drugs should be given, and in the cases that do not respond to sulfonamide therapy, local treatment be continued. I feel that a report and a recommendation should be made to the general practitioner as to how he should carry on the treatment of syphilis at present until penicillin or the more rapid methods are made available to him.

The Chairman: It seems to me that this is a desirable charge for the committee to consider for incorporation subsequently, although the Chair is open to discussion on this point. This can be held for additional study by the committee to be the subject of a subsequent report.

Comdr. Tony Fears (New Orleans, La.): I am sure that most of us were not able to digest all of the recommendations that were made. I should like to ask Dr. Neilson to read the one about postwar control of venereal disease to take care of the men who are being demobilized from the Army and Navy. If I understood it correctly, it was a recommendation that some organization, the government or otherwise, be charged with that duty. It seems to me that should be elaborated upon. There is enough distortion today between medicine and the Public Health Service; how is that going to be accepted by the practitioners of medicine? I should like for him to read that particular statement again.

The Chairman: Dr. Neilson, will you read that statement again, please?

Dr. Neilson: "The following motion was unanimously adopted by the Syphilis Section:

"That the cooperative study of penicillin in early and late syphilis under the general auspices of the Committee on Scientific Research and Development, in participation with the United States Army, Navy, and Public Health Service, be continued for a period of 5 years from now, or until adequate data have been obtained as to optimum methods or doses. Further, when the total demobilization of the armed forces occurs at the cessation of hostilities and the financial support of these studies thereafter ceases, the cost of the continuation of this program should be assumed by another organization,

governmental or otherwise."

The Chairman: Is there additional discussion of this or other points?

Dr. Lee Edens (Austin, Tex.): I am not entirely clear as to the recommendation on asystematic latent symptoms. About 70 percent of my syphilitic patients are of that type. I should like to know just what the consensus is on that point.

The Chairman: Is there a recommendation to that effect, Dr. Neilson?

Dr. Neilson: On the subject of late syphilis, under the heading of "Penicillin," the following recommendations were made:

1. Penicillin has little or no effect on reversing fixed positive blood serologic reactions.
2. Penicillin has an arsenic-like effect and will probably replace arsenic, particularly the pentavalent arsenicals.
3. Penicillin has a striking effect in grade I and grade II spinal fluids, and its efficacy in grade III spinal fluids is inversely proportional to the duration and extent of the infection.
4. Treatment of grade III spinal fluids with 2.4 million units of penicillin in 7½ days is justifiable. Initial doses should be reduced to prevent reactions.
5. The effect of penicillin plus fever in late syphilis has not been determined.
6. Treatment resistant central nervous system cases sometimes respond to penicillin.
7. Preliminary evidence indicates that early cases of tabes and paresis are clinically improved by penicillin therapy.
8. Preliminary evidence indicates that penicillin is effective in acute syphilitic meningitis.

In other words, for the general practitioner, until further study and observation have been done, there will be for the present no radical change in therapy.

Dr. E. G. Clark (St. Louis, Mo.): I should like to suggest that this last statement made by Dr. Neilson be incorporated as a recommendation. In answer to Dr. Goldstein and to many others who have asked that question, we recommend no change in the type of treatment schedule that has been in operation for the past several years. This conference, in regard to treatment, is speaking entirely in terms of rapid treatment centers, or centers in which rapid treatment may be given. I think it is unfortunate, however.

The Chairman: Would you like, Dr. Clark, to make that in the form of a motion?

Dr. Clark: Yes.

The Chairman: It has been moved and seconded that the last statement of Dr. Neilson be incorporated in the report to the effect that there is no significant change in the treatment of latent syphilis. The question? All in favor say "aye". Opposed. Carried.

Is there additional discussion of this report?

Dr. F. G. Gillick: (Washington, D. C.): I should like to request that Major Rein put into the form of a motion his suggestion concerning biologic false positive. I do not believe that Dr. Stokes' suggestion along that line was as clearly presented as it might have been.

The Chairman: Is there discussion of this point?

Dr. Stokes: Of course, I am allergic to the problem of biologic false positive because I spent a year of what remains of life finding out what a problem it really is. It is not reducible to such beautiful simplicity as Major Rein reduced it, if I may venture to say so after a year of living, eating, and sleeping the stuff. It is desirable perhaps that some recommendation be made in this report regarding practical simplified methods for the interpretation of biologic false positive, but I think it ought not to wipe out a broader general statement such as I ventured.

My fingers have been burned too much for me to attempt before a session like this to define the simplified methods of recognizing biologic false positive, and I think the problem is more complex even than Major Rein's statement suggests.

The Chairman: Is there additional discussion of this or other points of the report? If not, it has been moved and seconded that the report as submitted by Dr. Neilson, as Chairman of the Section, be adopted. Question? All those in favor say "aye". Opposed. The "ayes" have it and it is so adopted.

We will now hear the report of the Section on Epidemiology by Dr. N. A. Nelson, Chairman.

REPORT OF SECTION ON EPIDEMIOLOGY

Chairman: N. A. Nelson, M.D.,
Deputy State Health Officer
Division of Communicable Diseases
Maryland State Department of Health
Baltimore, Md.

Secretary: Robert Dyar
Lieutenant Colonel, (MC)
United States Army Air Forces

Dr. N. A. Nelson: It was necessary before proceeding with the work of this Section to define its limitations. Since epidemiology is the science of infectious disease, it is concerned with the total host-parasite relationship. Actually, therefore, the Section might have concerned itself with the entire natural histories of these two diseases without fear of having overstepped any scientific boundaries.

Practically, of course, so comprehensive a review of the epidemiology of gonorrhea and syphilis would be out of the question at such a conference. Much of it is common knowledge; some of it is the special concern of other participants in the conference, and much of it must await the outcome of research.

For these reasons, the Section has confined its attention to a few problems in the practical application of epidemiologic procedure in the field with which the health officer is especially concerned:

1. The conflict between nomenclature and sound epidemiologic procedure, and the confusion which therefore surrounds all attempts to measure the results of contact investigation and case holding.
2. The inadequacy of most of the methods now in use for measuring progress in the control of gonorrhea and syphilis.
3. The inadequacy of current case-finding procedures, particularly in view of the rapid curative effect of penicillin and certain other therapies.
4. The need for complete review of case holding under these newer therapies.
5. The chaotic condition of epidemiologic report forms and records.
6. The potential, if not immediate, importance of international epidemiologic procedure.
7. The need for prompt determination of what responsibility the health officer may have for making clear to the public the basic epidemiologic relationship between the spread of gonorrhea and syphilis and sexual promiscuity.

Before reporting the results of the discussion of these problems, it seems reasonable to state, somewhat more specifically, just what there is about them which demands our attention at all.

1. **The conflict between nomenclature and sound epidemiologic**

procedure and the confusion which therefore surrounds all attempts to measure the results of contact investigation and case holding.—It is time to inquire whether the definition of early syphilis as "any infection of less than 4 years' duration" serves the most practical purpose. Although it is true that the disease may become infectious, through recurrence and relapse, at any time during the first 4 years (and occasionally thereafter), most infections are communicable only at some time during the first year or two. The current definition of early syphilis may have broad statistical value, but it creates a serious problem when applied to case finding and case holding.

Will any experienced epidemiologist go so far as to suggest that any other than familial contacts (which may have to be followed regardless of the duration of the disease) can ordinarily be identified and brought to medical attention once the infectious period has receded more than a very few months into the past? Where is the patient who can recall his promiscuous sexual experiences over a period of 4, or 3, or 2 years, or even 1 year in most cases? Yet, the present definition of early syphilis implies that such case finding can be done without regard to when the disease was last infectious.

Furthermore, under this definition it is implied that intensive case holding must be undertaken throughout all of that period. This either places a burden upon case-holding facilities which is far too heavy for the protection of the public health which results, or leads to lowered morale by creating a case load which cannot possibly be carried. Is it not possible that, outside of research centers, intensive case holding may be limited to a considerably shorter period, in the light of what we now know as to when recurrence and relapse are most likely to occur?

Will it be necessary to have one definition of early syphilis for the statistical statement of the total of potentially infectious syphilis, and another under which to establish a rational range for case finding and case holding? Or should this gilding of an inherently imperfect statistical lily be sacrificed altogether, in order that more practical epidemiologic ends may be served? What is a practical definition of early syphilis?

The need for redefinition of the terms "case" and "contact" is urgent for, as they are currently used, they seriously interfere with the accurate measurement of epidemiologic accomplishment. The designation, case, must properly depend upon the completion of a diagnosis. Those persons who apply for examination, but who are found, eventually, not to be infected, may not be counted as cases, although provision should be made for crediting the medical agency for the work which must be done. However, if evaluation of epidemiologic accomplishment is to mean anything, it must be upon the basis of cases of diagnosed disease.

Strict adherence to this definition of a case will at once make it incongruous to apply the term, case holding, to the effort which is put forth toward keeping patients under observation until the diagnosis can be made, or infection ruled out. The use of this term should be restricted to the process of keeping a diagnosed infection under treatment control and posttreatment observation. What, then, shall the prediagnostic control of the patient be called?

How to define a contact is still more confusing. Although many persons may be identified as having been in intimate and sexual contact with the infected patient, and may require follow-up, they may not have been exposed to his disease. The intervention of prophylaxis, the indeterminate incubation period of a given infection, the fact that some contacts may have acquired their infections somewhere else before or since the exposure in question occurred, and various other considerations make impossible any exact estimate of the risk of infective contact until after the investigation is complete. Even then, failure of some diagnostic procedure may stand in the way of any final solution of the epidemiologic problem.

It is necessary, however, to distinguish between those "contacts" who are not infected or whose infections are not related to that of the "original case," and those contacts whose infections are so related. The final measure of epidemiologic accomplishment must be expressed in terms of infections found, not in terms of the work which was required to find them. Yet the agency which has been careful to trace and examine as many potential infective contacts as possible should be credited with having made a thorough search. All this requires a system of complicated bookkeeping which adds to the confusion.

The confusion becomes chaos when any attempt is made to differentiate epidemiologically between an infected contact and a case. To illustrate: A male seeks medical advice for a urethral discharge and a diagnosis of gonorrhea is made. A case of gonorrhea is entered upon the books, and an effort is made to identify the contacts. Two females are discovered to have been in sexual contact with the patient within the limits of the incubation period of the disease or subsequent to its onset. One of these is the patient's wife. These 2 women report to the clinic, are examined and found to be infected. They are entered upon the books as contacts of the original case, and that half of the epidemiologic problem has been solved.

They are also entered on the books as cases, however, since the diagnosis of gonorrhea has been made. Their contacts must be identified and found; both name the original male patient as their contact, and the lady who is not the patient's wife also names another male who happens to be under treatment in the clinic. Since both of these male patients are under medical care, there is no need for their further follow-up, and no entry of epidemiologic accomplishment can be made. Thus it appears, from the record, that the follow-up of female contacts of male patients has produced excellent results, whereas the follow-up of male contacts of female patients has been totally unproductive. All sorts of variations of this theme might be recited for both gonorrhea and syphilis.

It is obvious that the epidemiologic process is a completely reversible one. Cases become contacts and contacts become cases, and the further afield the investigation proceeds, the more interrelated these reversible reactions become. Both cases and contacts, no matter how they come to the attention of the medical agency, must be taken into account when the epidemiologic evaluation is made. Is it not possible that the entire epidemiologic problem around and including the infection which prompts the investigation

could be looked upon as an epidemiologic unit, and the result of the investigation stated in terms of the degree to which the entire problem has been solved without regard to how any particular infection came to attention?

2. The inadequacy of most of the methods now in use for measuring progress in the control of gonorrhea and syphilis.—Gonorrhea is essentially an acute disease. Those cases which are not counted within the statistical year of their occurrence are not likely to be counted at all. Syphilis, on the other hand, being a chronic disease, may be counted in any year of its long duration that it becomes detected.

Measurement of progress in the control of gonorrhea requires that enough of the cases which occur be counted each year so that the trend of incidence may be determined with reliability.

There are two great difficulties in the way of making sufficiently accurate counts. First, although most infected males are promptly aware that something is wrong, legitimate medical attention is often not sought; if obtained, the diagnosis either is not made or is not reported in too many cases. The reservoir of uncounted cases is therefore so great that wide fluctuations may occur in the count from year to year and so completely obstruct any attempt to determine a trend of incidence. Apparent trends may reflect nothing more than the trend of reporting, there being a rise with stimulation of interest, and a fall with lack of stimulation. The result is that we know nothing about the incidence, or trend of incidence, of gonococcic infection even in males. Second, gonococcic infection in females is too often impossible of diagnosis without repeated culture of carefully collected specimens, and may be missed even with culture. Morbidity reports, therefore, have so far had little value in the measurement of progress in either direction, that is, backward or forward.

Since most urethritis in males is due to gonococcic infection, and since most males must be aware of a urethritis from any cause, might it not be possible to sample certain groups of males from time to time to determine the incidence of urethritis during any given period, and so arrive at a trend? Could we afford to put all of our effort into such a measurement as this, to the exclusion of all other obviously futile analyses of morbidity reports and other data? We have spent a tremendous amount of time and money in our attempt to obtain information which has not been forthcoming. May it not be time to abandon fruitless traditional procedures for what might be a more productive innovation?

The measurement of progress in the control of syphilis is still more difficult as to incidence of fresh infections, but may be more possible because of the element of time which permits the more leisurely determination of prevalence of infection regardless of duration.

For many reasons, a large proportion of those infected are not promptly aware that they have acquired syphilis. Early lesions may be absent or apparently of little consequence, or hidden, or interpreted as due to other causes. It is not likely that this situation will improve rapidly. As long as only a small fraction of the total of new infections is detected and counted when early, the same possibility of wide fluctuation in reported incidence, which

operates to obstruct any reliable estimate of trend of incidence of gonorrhea, will also operate here. The only hope for an approximately accurate measurement of trend lies in the determination of disease prevalence.

One excellent base line has already been drawn for the prevalence of syphilis in a large part of the population, through the examination of men for Selective Service. It does not matter very much that comparable data are not available for the higher or lower age groups or for females. What happens in this large body of men should reflect adequately what is going on in the community.

However, this base line will be of little use for the determination of a trend unless there is another war and a new measurement of prevalence can be obtained; or unless it is possible to continue the sampling in peacetime on a more restricted but equally representative basis. Might it not be worth while to discard morbidity reporting of gonorrhea and syphilis altogether, and depend upon soundly devised group sampling to tell us where we are going? What would actually be lost to us by such a procedure?

3. **The inadequacy of current case-finding procedures, particularly in view of the rapid curative effect of penicillin and certain other therapies.**—A man may be exposed to gonorrhea on Sunday, infect his wife on Monday or Tuesday, discover that he has been infected on Wednesday, complete his treatment with penicillin in time to renew his sexual activities on Thursday and discover, on the following Sunday, that he has been reinfected by his wife, if not by someone else. If weeks are substituted for days, somewhat the same sequence of events may be expected if a recently acquired infection with syphilis is treated with penicillin, or by any of the other rapidly administered therapies.

It is no longer sufficient, therefore, to place the patient under medical care and defer for long the treatment of the contacts. Our case-finding procedures must be stepped up to meet this new speed of cure; this great new risk of prompt reinfection must be considered in education of the patient. Can epidemiologic investigation be accelerated to the point of adequate effectiveness? Are there sources of epidemiologic manpower not yet tapped or fully utilized to which we may turn for assistance? What shall we do about case finding when the newer therapies are available to every physician and the cost is so low that the infected will flock to private medical care? Shall we be obliged, as one observer has suggested we may, to advertise everywhere the easy availability of quick cure, forget epidemiologic investigation, and spend all of our time on public education for the detection of infection, and on the provision of medical care?

4. **The need for review of case holding under these newer therapies.**—The treatment of gonorrhea with penicillin has already reached the point where the need for case holding for observation after treatment may be very much in doubt. If a patient can be cured in a matter of hours, with almost no risk of relapse or of producing an asymptomatic carrier state, posttreatment observation will be a waste of time. It will have little value in the evaluation of the drug because reinfection will be promptly possible in ambulatory patients.

What the case-holding problem will be for syphilis under the

newer therapies will have to await adequate information as to the lowest obtainable relapse rate. That, in turn, will have to await determination of the most effective dose of penicillin and the most effective combination and method of administration of other therapies. Even now, however, it may be possible to limit posttreatment case holding to that period during which it seems most likely that relapse may occur. Can recommendations be made, now, as to reasonable limitations which may be placed upon case holding?

5. **The chaotic condition of epidemiologic report forms and records.**—The forms currently in use throughout the United States for interstate epidemiology are becoming constantly more complex and confusing. There are State health department forms and local health department forms; there are Army, Navy, and Coast Guard forms; there are forms from anyone anywhere who wants a contact traced or a patient transferred; there is now the United States Public Health Service Separation Epidemiologic Form, which is not satisfied with inquiring whether the soldier was brought to medical attention, but must also know how many fruitful and fruitless visits, how many letters, and how many telephone calls were made to accomplish the desired end.

There is such a profusion of sizes, colors, numbers of illegible carbon copies, items to be scanned, and items to be reported that life for the harassed health officer and his overworked staff must be one continuous nightmare. Some of the time he must keep copy A and return copy B; some of the time he must keep copy C and return copy B. Some of the time there is no copy for his own record for which he should be everlastingly grateful, for none of them will fit into any of his files.

There are "all-purpose" forms, apparently designed to satisfy the requirements of some central tabulating unit. These are filled from end to end from top to bottom with innumerable spaces, some filled, some to be filled and some to be ignored. All of these spaces are cluttered up with annoying code numbers.

Too much thought has been given to the desires of statisticians for more and constantly more figures to play with, without regard to what may reasonably be requested, or what practical end the analysis of the data collected could possibly serve. Might it not be possible to devise a simple, uniform, single-purpose form for interstate use? And in the devising of it, might not a few local health officers be consulted as to what information of practical value they could be expected, reasonably, to supply?

6. **The potential, if not immediate, importance of international epidemiologic procedure.**—Gertie of Bizerte may soon become a serious source of infection of males who, since travel has become so swift, may return to this country within the incubation period of either gonorrhea or syphilis. There is a growing impression that gonococcic epididymitis is becoming more common than it has been for many years, and in a form which is slow to respond, even to penicillin. This complication is said to be very common in Italy, due to the misuse of the sulfonamides by the promiscuous female population. Have some of these already invaded this country? In what other directions must we look for new epidemiologic complications of our complex problem of genitoinfectious disease control?

With the certain development of commercial airplane travel,

it is reasonable to believe that speed will join hands with disease to make it our concern as to what is going on elsewhere in the world for the control of gonorrhea and syphilis. What should we be doing toward the establishment of quick and effective epidemiologic working-relationships between health authorities everywhere?

7. The need for prompt determination of what responsibility the health officer may have for making clear to the public the basic epidemiologic relationship between the spread of gonorrhea and syphilis and promiscuous sexual intercourse.—There is a growing disposition on the part of some of the people of this country to condemn the health officer for teaching people the medical facts about gonorrhea and syphilis and their prophylaxis, to the exclusion of any adequate discussion of the relation of these diseases to human sexual behavior. These people have short memories, for it was only 8 years ago that this serious public health problem could be brought into the open at all, and then as one of communicable disease control. The public would not then have tolerated what it would have considered brazen and indecent discussions of sex behavior. No health officer need apologize for the effort which he has put into making the control of gonorrhea and syphilis one of the principal "musts" of public health work. He will, in fact, have much to account for if he permits it to drop into oblivion after this war, as he did after the last one.

It is an unescapable epidemiologic fact that if it were not for sexual promiscuity there would be no problem of genitoinfectious disease control. We cannot forever publicly ignore this fact without implying that we can, by epidemiologic and medical means, control gonorrhea and syphilis no matter how promiscuous people may be. We have hinted that there are degrees of promiscuity which spread disease much faster than any public health procedure can overcome it, by insisting that no program for the control of these two diseases can succeed in the presence of tolerated prostitution. We are rapidly becoming of the opinion that the high rate of infection in the Negro will finally respond only to improvement in the social and economic opportunity of the Negro; that it is more a social problem than one of communicable disease control. As one of the participants in the discussion in the Section meeting put it, "* * * it is probably true that prostitution has always been a more important problem in itself than it was a source of venereal disease spread. Yet, by and large, it has not been possible to stimulate interest in the problem except on the basis of the control of venereal disease, and this usually during wartime. Similarly, high venereal disease rates in slums and the underprivileged groups have frequently attracted more attention than did the slums and the underprivileged groups themselves. But it should be clear now that venereal diseases are significant only as an index of the culture of the people in which they are found, and are related to the level of education, adequacy of medical care, living conditions, sexual customs and habits, etc. * * * If the sociologists, the psychologists, and the theologists can find no better argument against promiscuity than venereal disease, then it would appear that the subject had best be allowed to sink into oblivion." England and the Scandinavian countries have discovered that the dis-

turbance of male and female relationships which arise out of war can at once overcome everything which has been gained by a peacetime genitoinfectious disease control program.

We would be condemned, as health officers, if we implied that we could, by epidemiologic procedure and therapy, control typhoid fever no matter how thoroughly the public was convinced that it should have the privilege of drinking from a dirty water supply. We may not build, nor run, the water purification system, but we everlastingly and loudly proclaim that unless the water supply is cleaned up, there will be both endemic and epidemic typhoid fever. We owe it, likewise, to the public, when the time comes that we can do so without the risk of driving the whole subject back under cover, to make clear the relationship between genitoinfectious disease and sexual promiscuity. Perhaps the time has come when we should begin to do so.

Better human male and female relationships have a far greater value than the mere control of disease. Sexual promiscuity strikes at the very roots of the family—the basic unit of our form of civilization. The responsibility for finding the solution of this great sociologic problem lies with the home, the church, the school, and the agencies in the community which should be concerned with character building. It does not lie with the health department. However, it does lie with the health department to tell people that it has more than adequate evidence that there is something wrong with human male and female relationships in the incidence of gonorrhea and syphilis; neither of these diseases would exist if it were not for sexual promiscuity. What people then decide to do about it is their business.

It may be particularly important to raise this issue now. If overnight cures are to be available for both gonorrhea and syphilis, they may cease eventually to be important public health problems, not because they may be less often acquired, but because they may be inexpensively cured before causing serious damage. Their high incidence may still reflect widespread sexual promiscuity, but whether or not anything is done to repress the poor behavior will be of no epidemiologic concern to the health officer. Perhaps those who should have been interested in this large problem of human behavior will then be forced to take over. What should be our position in the matter now?

The Section, having deliberated upon these questions, offers the following opinions, conclusions, and recommendations:

1. As to the conflict between nomenclature and sound epidemiologic procedure, and the confusion which therefore surrounds all attempts to measure the results of contact investigation and case holding.—While it was the consensus of the Section that the definition of early syphilis should remain as it is, for broad epidemiologic and therapeutic purposes, it will be necessary that the epidemiologist use discrimination in practical case finding and case holding, to the end that effort will not be wasted in attempts to reach too far beyond the period of infectiousness of the disease.

It was the consensus of the Section that much of our epidemiologic terminology is confusing and that unless it is redefined, reasonably accurate evaluation of epidemiologic accomplishment will be impossible. It is particularly important that such terms as

case, contact, case finding, and case holding be clarified as to their true epidemiologic significance. When this has been done, it may be possible to devise simple and practical indices for the expression of epidemiologic accomplishment, and to determine whether this accomplishment can better be expressed on the basis of epidemiologic units than as new infections found per so-called "original case."

Since the solution of this complex problem was impossible within the time limits of the Section meeting, it is recommended that the United States Public Health Service select an Advisory Committee on Epidemiologic Procedure. One of its functions will be to determine, in consultation with representative State and local venereal disease control officers, whether or not practical and acceptable definitions of these terms can be evolved, and adequately simple indices of epidemiologic accomplishment be devised.

Although it was generally agreed that the most useful information as to incidence, prevalence, and trends has come out of group studies, such as serologic surveys of selectees, pregnant women, candidates for marriage, et cetera, and that these group studies should be continued, it is felt that morbidity reporting is of sufficient value, especially for stimulation of public interest, to warrant its continued use. Accurate appraisal of trends in the incidence and prevalence of the venereal diseases must depend upon carefully conducted and well-controlled studies of selected population groups, the studies to be repeated from time to time. Research is as essential in epidemiology as in clinical and laboratory medicine.

2. The inadequacy of current case-finding and case-holding procedures, particularly in view of the rapid curative effect of penicillin and certain other therapies.—Here, again, is a problem too complex for solution in a small part of an afternoon. It is recommended that detailed consideration of this problem be another function of the proposed Advisory Committee on Epidemiologic Procedure.

It was the consensus, however, that much time and effort are wasted in essentially nonproductive procedures which might better be utilized in certain specific forms of case finding. Predominant among the suggestions arising out of the discussion were:

(a) The need for determining more exactly when field visits for case holding should give way to administrative follow-up by letter, telegram, and telephone, and in what cases field visits and administrative effort should not be made.

(b) The need for determining which areas of case-finding effort are productive and which are not, with the view to the abandonment of the latter.

(c) The need for review of the practice of making return reports of results in interstate contact investigation. What useful purpose do these return reports serve a State in which the alleged contact does not live?

(d) The need for elaborating a general acceptable policy with reference to the treatment of patients with gonorrhea, (especially female patients) on the strength of epidemiologic and clinical findings. Unless such a policy is adopted, there will be little point to case-finding attempts since failure to obtain laboratory confirma-

tion of the diagnosis will very often nullify the case-finding effort.

The Section was in general agreement that with the advent of penicillin therapy, contact investigation must not only be intensified in order that more new infections may be found, but that it must also be greatly expedited in view of the great possibility of prompt reinfection. This is of the greatest importance in the control of gonorrhea, since reinfection may occur within a few hours after the initial infection has been diagnosed and treated. It will doubtless prove to be as important in the control of syphilis when we have accumulated adequate information as to the time and rate of reinfection following rapid treatment therapy.

Considerable doubt was expressed as to the value of case holding in gonorrhea after penicillin therapy, except for the purpose of determining whether infection with syphilis has also occurred. It was the consensus that effort now being devoted to such activity would be more productive if directed to case finding. Whether or not a similar conclusion can be reached as to case holding in syphilis after rapid treatment will depend upon further findings as to the rate and time of relapse.

It was the further opinion of the Section that in order to intensify and expedite case finding, the fullest possible use should be made of all available health department personnel. Interesting reports of the effectiveness of even part-time health officers in this procedure were available, the only need being that they be given basic instruction for stimulation of interest. The Section believes that much thought must be given to the matter of epidemiologic investigation in private practice for, when penicillin becomes readily available and less expensive, there will doubtless be a drift of those infected to private physicians and away from organized case-finding facilities as they are now set up.

3. **Epidemiologic report forms and records.**—The Section was unanimous in its expression of appreciation of the effort which has been made by the United States Public Health Service to standardize and simplify forms, and especially those used in interstate contact investigation and case holding. It was felt, however, that there is still room for improvement. There is still too great a profusion of types of forms, too great variation in their content, and too much attempt to collect information which may have some remote statistical interest but which is impossible to obtain. There is inherent in any standard form, a danger that those who are to supply the required information may resort to mechanistic, instead of intelligent, interpretation of what is sound and useful information. Differentiation must be made between records which are to serve as a guide to administrative action or to be used for historical purposes, and records which are to provide data for research.

It is recommended that the proposed Advisory Committee on Epidemiologic Procedure give its attention to the further simplification of working forms, and that in so doing it consult with those who are ultimately to supply the information in the field. These forms should be so devised that analysis of the data collected will serve primarily to help the health officer and his staff to do better work in the field.

4. **International epidemiology.**—In view of the universal exist-

ence of venereal disease, the rapidly increasing availability of facilities for more rapid international transportation, and the great probability of an increasing incidence of venereal disease in those populations physically and emotionally dislocated by war, international collaboration in venereal disease control is essential. The demonstrated success of the Allied Armed Services in such a cooperative effort should serve as a source of encouragement to other agencies.

International cooperation should include international exchange of technical material and epidemiologic data, including information relative to the facilitation of the spread of venereal disease. The problem of venereal disease control should be viewed on a global basis, and there should be constant global evaluation of trends, of program content, and of control strategy.

To this end, some form of international venereal disease organization should be provided, and provision should be made for periodic assemblies for the full discussion of the problems involved.

5. **The need for redefining public health practice in the light of the relationship between sexual promiscuity and the spread of gonorrhea and syphilis.**—It was practically the unanimous opinion of the Section that:

(a) One responsibility of the health officer is to attempt the control of gonorrhea and syphilis by epidemiologic investigation and therapeutic procedures.

(b) It is the further responsibility of the health officer to appreciate that if it were not for sexual promiscuity there would be no venereal disease.

(c) Further, it is his duty to make the epidemiologic relationship of sexual promiscuity to venereal disease known to every person within his jurisdiction.

(d) It is his duty, therefore, as a health officer and a good citizen to aline himself with those forces in the community which are concerned with the improvement of human male and female relationships for the sake of better morality and the preservation of the family as the basic unit of our civilization. He must know that the solution of this broad and fundamental problem contains the ultimate solution of his own disease control problem.

It was equally the opinion of the Section, however, that the health officer should firmly and conclusively reject the implication, so consistently expressed, that the control of venereal disease is either the sole or the primary objective of social hygiene. This is implied by all current opinion and practice.

The police are called upon to repress prostitution, not because prostitution, *per se*, is harmful to society, but because it spreads disease. The repression of prostitution is made a wartime "must" only because it contributes, through the spread of infection, to serious manpower loss. The armed forces are concerned with the belated instruction of the youth of our nation in good sexual behavior primarily in order that disease may be prevented and valuable manpower saved.

Juvenile delinquency is deplored, especially in wartime, more because it spreads gonorrhea and syphilis than because of what it does to the integrity of the family and to the structure of our society.

Facilitators of sexual delinquency are condemned not so much because they facilitate sexual delinquency, but because sexual delinquency spreads disease. So long as no contact investigation points the finger of disease facilitation at him, the tavern keeper and his clientele remain unmolested. The many "hot spots" and their promiscuous hangers-on specializing in the defense worker, for whom there is no organized system of contact identification, are evidence of this fact. They fear no community action.

It is urged that sex hygiene be included in the school curriculum, not so much because sex character building is important to us in its own right, but because it is necessary to teach children, before they are likely to become exposed, that sexual promiscuity results in infection.

The church, which has so far failed to teach people how to live together as males and females, as evidenced by the size of the problem of venereal disease, has permitted itself to become involved in the public discussion of sex behavior only because of the urgency of the public health problem. Even the American Social Hygiene Association is far more generally known for its activities in the prevention and control of gonorrhea and syphilis than for what it has done to strengthen our moral fiber and to secure the position of the family as the fundamental unit of our civilization.

The public in general has been thoroughly convinced by this universal clamor for venereal disease control that this is the sole objective of the social hygiene program. In fact, in order to bring any part of this great problem into the light, Surgeon General Parran was obliged to introduce it in 1936 as one purely and simply of communicable disease control.

Carried to its logical conclusion, this line of reasoning must lead to the saddling of the health officer with the direct and official responsibility for the repression of prostitution, the control of juvenile delinquency, the teaching of sex hygiene, and the promotion of sex character building. As a matter of fact, police departments have been employed largely, in the last war and in this, as agents of the health department for the sole purpose of screening disease out of prostitution and promiscuity. Those found not to be infected are permitted to pursue their promiscuous ways. Even the courts determine the guilt or innocence of the prostitute on the basis of the positivity or the negativity of a blood test.

Carried to its ultimate conclusion, this approach to the problem implies that when gonorrhea and syphilis cease to be important as public health problems, there should be no further objection to prostitution and promiscuity in any degree. There is no escaping that conclusion. It will hold whether those diseases are actually exterminated or only reduced to economic and pathologic insignificance by cheap and easy cure, the incidence of new infection remaining as high as before.

It was the consensus of the Section that those forces in the community which should be interested in strengthening our moral fiber and in securing the position of the family as the most important element of our civilization, should find in those objectives the fundamental stimulus for doing something about sexual promiscuity and about the correction of those social conditions which promote and facilitate sexual promiscuity.

Gonorrhea and syphilis are symptoms of a social condition which threatens something far more important than the health of our people—the structure of society itself. To treat this symptom to the neglect of the more serious, basic condition would be as reprehensible as to prescribe aspirin for a headache and let the causative brain tumor go; or worse, to remove just enough of the tumor to relieve the pressure and cure the headache.

We must not permit those upon whom this larger and more fundamental community responsibility rests to unload that responsibility upon us by the legerdemain of making the symptom appear to be the basic disease. We shall be guilty of the gravest malpractice if we permit ourselves to be persuaded to assume a responsibility which is obviously first that of the church, the home, the school, and every other character building agency in the community, and only secondarily an epidemiologic responsibility

Dr. Nelson: I move the adoption of this report.

The Chairman: It has been moved for the adoption of this report. Do I hear a second? Seconded by Colonel Dodge. The report is now open for discussion.

Dr. James H. Lade (Albany, N. Y.): You have heard that the Section did not vote to change the definition of early syphilis. The definitions which were under discussion were to define all syphilis of less than 4 years' duration or of less than 1 year's duration as early, with the implied connotation of communicability. I believe that the only reason for retaining the classification including 4 years was the desirability of holding the patient, admitted in the clinic during that period. I think it only fair to say that there was a small but determined minority who felt that syphilis of less than 1 year's duration or cases of less than 1 year's duration included most of the infectious syphilis, at least for contact investigation. It is certainly true that it is rare that one finds a patient in his second, third, or fourth year of infection with definite physical evidence of communicability at the time of admission to the clinic.

I wonder whether it would not be possible to reconcile the differences in the contact investigation approach to syphilis and the clinical necessities of keeping the patient already found under treatment by defining early, or if we should use the term "communicable syphilis" as of less than 1 year's duration, and stick to the policy of holding patients who are in their second, third, and fourth year, without implying that communicability or transmission of the infection by contact between adults is probable.

I wish to bring up for discussion in the general session an amendment to the report of the Section that early syphilis can be defined as the general disease, that is, that communicable syphilis be defined to be of less than 1 year's duration.

Dr. Nelson: I think that many of us, or some of us at any rate, felt as Dr. Lade has expressed himself, that the use of the definition of early syphilis as a disease of less than 4 years' duration might serve some statistical use, as I said in the preamble to my report, but that for practical purposes it was really confusing. I should like to recommend that this definition be amended.

The Chairman: Is there any additional discussion on this point? Dr. Nelson, do you make that in the form of a motion or an amendment?

Dr. Leon S. Saler (Surgeon, U. S. Public Health Service, State Health Department, Baltimore, Md.): I move to amend the recommendation in such fashion that the definition of early syphilis be defined with respect to case finding and case holding as being syphilis of 1 year's duration or less as opposed to the procedure which we have now for therapeutics and everything else which is 4 years or under.

The Chairman: You have heard the motion by Dr. Saler, or the amendment to the effect, that for case holding, case finding, and epidemiology early syphilis be considered of 1 year's duration or less. Is there a second to that motion or amendment?

Dr. Hollister seconds the amendment. It is now open for discussion. Question? Those in favor please say "aye"; opposed. I think we should have a

rising vote on that. Those in favor of the amendment please rise; those opposed to the amendment please rise. I suspect that we had better have a count. I should like additional discussion. It seems to me that with the lack of unanimity on this point, there might be additional discussion.

Dr. Gillick: Dr. Saler added a point that I think is well worth considering. He stated for purposes of case finding and case holding this definition be accepted. I should like to say that for the purpose of this particular phase of public health work in venereal disease control that definition is a practical one, but for the purpose of looking upon syphilis as wholly limited to being possibly infectious or relatively infectious only to the first year, I would object. I do not believe that we have sufficient evidence to state that we absolutely know, and if it were limited and specified that it was only for the purpose of interviewing such patients and obtaining the contact information from patients with syphilis under 1 year, I believe it would be reasonable.

The Chairman: Is there additional discussion?

Dr. Vonderlehr: I do not believe that we are going to be able to settle this question regarding the epidemiology of syphilis, that is, the length of time that a patient with syphilis remains communicable. I recall very well that about 5 or 6 years ago the Public Health Service organized a study of the period of communicability of syphilis. The Cooperative Clinical Group and a number of other workers were engaged in this study. We spent probably $25,000 or $30,000 at that time, and at the end of 2 or 3 years' investigation, we learned that it was impossible to say just when the period of communicability ended. There are a number of factors involved, but the most important one that added to our complications was what we dubbed the "iceman factor," the question of whether or not people actually had illicit or sexual contact when they alleged they had not.

This entire problem of sex behavior is so complex that I think we might argue from now until doomsday, without furthering scientific advancement, and not get the answer. However, it seems to me that from the standpoint of epidemiologic investigations and based on the experience that most of us have had with reference to syphilis, the limitation of 1 year as the maximum period of communicability is satisfactory.

Dr. D. C. Smith (University of Virginia, Charlottesville, Va.): At present, following the modified intensified therapy program, we do not know the length of time that elapses. It may be 6 months, 12 months, or 18 months. For that reason I think it would probably be bad to put a definite calendar limit on your health work. I think Dr. Nelson's original statement, where he emphasized leaving it to the discretion of the physician and the health officer, is of more importance.

The Chairman: Additional discussion?

Dr. Lade: May I again suggest an amendment to the amendment to reconcile the sincere differences of opinion, that this definition apply only to untreated syphilis? Obviously a treated case, where varied schedules are in force and where the patient is in a clinic, may be determined by clinic policy.

In answer to Dr. Gillick's criticism of transmission in the second, third, and fourth year, there was no intent in this suggestion to imply that transmission is impossible after the first year but, rather, less probable, and that we need to concentrate our efforts on the patient most likely to transmit his infection.

Could we then redefine this to the general satisfaction of everyone as communicable or infectious syphilis, unqualified so long as it is untreated, as one less than 1 year's duration, and the second, third, and fourth year as potentially infectious?

The Chairman: Dr. Saler, would you consider that amendment to your amendment?

Dr. Saler: I would prefer not to do so. I believe that introducing the element of treatment, of whether the case has been treated or not, will be confusing to the workers in the clinic, and I would prefer to leave that to someone not in uniform. For practical purposes we should define early syphilis as under either 1 or 2 years and that it has to be with or without treatment. In other words, the same horse has to have the same color all the way through. I think the introduction of the treatment factor would cause confusion.

The Chairman: Is there discussion on this point?

Dr. William G. Hollister (Passed Assistant Surgeon, U. S. Public Health Service, Supervisor of Venereal Disease Control, Jackson, Miss.):

I should like to ask if this also includes familial contact. Does that have to be interpreted differentially from the extrafamilial contact?

The Chairman: Dr. Lade, did you understand Dr. Hollister's question as to whether this includes familial contacts?

Dr. Lade: I had no intention to generalize concerning contacts but as to cases diagnosed as syphilis of a particular duration, however acquired, by familial or other contact.

The Chairman: Additional discussion on this point?

Dr. Irvine: It seems to me that there is no good purpose to be served by changing this definition to 1 or 2 years. I think that the nomenclature which has been established should be left alone rather than to change it and have people obey it arbitrarily. It is not necessary, it seems to me, for any health officer arbitrarily to say that every case that is within 4 years must be investigated for source and contacts. I see no reason he cannot interpret that anyway he likes from the standpoint of epidemiology, but it will make a great deal of confusion if it is limited to 1 or 2 years.

Those of us who have occasion in clinics to treat syphilis over a period of years know perfectly well that we are always meeting the unexpected syphilis, and to say that no syphilis recurs in the infectious stage within 1 or 2 years is entirely wrong. I do not believe that can be proved anywhere.

All of us who have had much experience in actually treating syphilis know that it may recur in the infectious stage in 10 or 15 years. We all know that a great many patients with syphilis, who are fortunate, may be cured in 6 or 8 months. The figures compiled many years ago demonstrated that, but we know that in order to make sure of the cure with our own kind of treatment, we have to give everybody the maximum. I think that applies to this situation, that we need a figure which is quite sure, so as to include the possibility of infectious relapse or continued infectiousness, in order to do proper epidemiologic work.

The Chairman: Additional discussion?

When the question was before the conference on Dr. Saler's amendment, it appeared to the Chair to be fairly evenly divided. It is quite apparent that no amendment can be carried to that extent. I wonder if it would not be wise, in view of the discussion, to put the question before the conference once more. The amendment is that for purpose of case holding and case finding, early syphilis be considered as of 1 year's duration or less. Those in favor please rise; those opposed to the amendment please rise. It will be the decision of the Chair that the opposition is in the majority. The report is open for additional discussion.

Dr. Wm. Guthrie (Lansing, Mich.): It seems to me that the main point of difference here has been more than a matter of words. The group is opposed to changing the definition of early syphilis. I voted against it and I am not opposed to the intent of this statement. I believe the purpose the committee had in mind can be achieved without a redefinition of early syphilis in terms of period of maximum communicability or the period in which contact investigation is most fruitful, or in words other than a redefinition.

The Chairman: The question? Those in favor of the adoption of the recommendations of this Section please reply by the usual sign of "aye"; opposed. It is so ordered.

[The meeting adjourned at 12:45 o'clock.]

SATURDAY AFTERNOON SESSION

November 11, 1944

The meeting convened at 2:10 o'clock. Dr. J. R. Heller, Jr., presided.

The Chairman: The report of the remaining Section, that on Education and Community Action, is to be delivered by the chairman, Dr. William F. Snow, of the American Social Hygiene Association.

Dr. William F. Snow: The Section on Education and Community Action was organized, for purposes of yesterday afternoon's meeting, with the speakers, Dr. Heller, Colonel Sternberg, Commander Schwartz, Mr. McCloskey and Dr. Clarke, as a panel of reference, and they were available in the course of the afternoon in reference to various questions which came up. Then we had Mr. Hardy[1], Captain Larimore, Lieutenant Ennes, Mr. Fink[2], and Miss Pinney[3] as an editorial group to join with Dr. Hazen in keeping references of those who spoke or expressed opinions and wanted to elaborate them afterwards.

We thought that if we adopted some such plan we would save time in reference to various proposals and could do what the congressman does in asking permission to expand his remarks in the record. So with that in mind, we secured the names and addresses of all the persons who were taking part in the Section, and we expect to turn over to Dr. Heller and his associates in Washington a good many notes and minutes and comments that are not complete, with the request that it be considered that our report this afternoon is a progress report and will be subject to such revision as may come out of further correspondence about these proposals.

[Dr. Snow and Dr. Hazen presented, as a progress report, an informal review and summary of the discussions and remarks which had taken place within the Section meeting the previous day.]

The Chairman: Dr. Snow, did you wish to move the adoption of the progress report?

Dr. Snow: I move its adoption as a progress report.

The Chairman: Dr. Snow moves its adoption as a progress report.

[The motion was seconded.]

The Chairman: It is moved and seconded that this progress report submitted by Dr. Snow and Dr. Hazen be adopted by the conference. We should like to have discussion upon this report.

Lt. Howard W. Ennes, Jr., (U. S. Navy, Washington, D. C.): As a layman, and let me emphasize that, I am still somewhat confused, even after all of the papers and the discussions in both the Education Section and the Epidemiology Section have been presented, as to the educational and public approach to venereal disease. I think there is still a great realm of misunderstanding as to our objectives. The conflict between our objectives for the treatment and the cure of venereal disease and the larger problem of promiscuity and the sexual problem with which we are dealing is apparent, although I do not think it is real. From my point of view, at least, we have not come out of this conference with a clear statement of our objectives. I do not think, from my little experience in public education, that we are going to be able to go forward much further until we get some clarification.

It is certainly true that we are dealing with a problem in venereal disease which is a small and relatively insignificant aspect of a total sexual problem which we face as a society. Insofar as venereal disease reflects rather specifically more or less an accident, because venereal disease infection is merely an accident, it seems to me as far as the total significance of promiscuity is concerned, we are dealing with simply a symptom of a basic social and personal disorganization. As the Epidemiology Section suggested, we need a reconsideration of our point of view so that we do not put the point of the triangle, so to speak, on venereal disease when we are really considering promiscuity. It seems to me that we need to give considerably more attention to the mental hygiene problem which venereal disease represents.

I should like to put this specific point into the discussion. It seems to me, as a layman, that we are coming into an era when treatment is basic. More

[1] Mr. Judson Hardy, U. S. Public Health Service, Washington, D. C.

[2] Mr. Arthur E. Fink, Federal Security Agency, Washington, D. C.

[3] Miss Jean B. Pinney, American Social Hygiene Association, Washington, D. C.

and more with our new methods of treatment, we are going to be handling an individualized treatment problem, having our patients in hand for a relatively short period of time; we cannot put too much stress upon the importance of handling that patient from an educational standpoint.

Looking at it in case-finding terms, we have two weapons to use. One is the matter of using education for bringing patients in to treatment; the other, more specific, and I would expect possibly more productive, that of contact investigation and all that it implies. In the Navy we consider any patient coming to a dispensary as a failure of our educational program specifically and of the control program in general. If we get that idea uppermost in our minds, we may be able to give a little more attention to the patient who, in our experience, is very likely to repeat his infection. In other words, I want to stress the importance of education with the patient in the clinic, in the treatment center, or wherever it may be.

It is certainly not too much to say that we have to develop in every physician and in every clinic worker an educator so far as the patient is concerned. These personal contacts with the individual should be put to practical uses. We can do a great deal there in venereal disease terms and possibly even in broader terms, but we are overlooking that now; we are overlooking it seriously in the services and in civilian experience. It seems to me that we need to give considerable attention to the in-service training of our own staff along that line.

I would like to mention one other point. The individual who comes in for examination and is found to be noninfected is as much an educational problem as the patient. The fact that an individual is a contact of a case or suspects that he may be infected certainly suggests to me that the chance of infection of that individual at some later date is reasonably high. You have a golden opportunity there perhaps to delay that time substantially. If you can show the way, shall we say, with facts and with motivation, it will be helpful to him.

The Chairman: It is open for additional discussion.

Dr. W. A. Mason (Atlanta, Ga.): The fact that the gentlemen said in their report that they do not know exactly how this matter of Negro education might be carried out gives me an opportunity to say something. I was interested in Dr. Stokes' remarks this morning that for a long time he had been living, eating, and sleeping with this matter of biologic false positives. Not by choice, but possibly because of convenience, for a number of years I have been living, eating, sleeping, and working with Negroes.

The Negroes, the intelligent Negroes at least, are not chagrined by the high rate of venereal disease among Negroes, but we rather accept that as a challenge to want to do something about it. We feel that we can do something if we are integrated into the over-all planning of public health programs, especially as they pertain to venereal disease; if we are taken in, actually integrated, give total integration in the over-all planning, we can take the plans back to our people and do a good job.

I think it is a truism that if you want to find rabbits you use a rabbit dog. In my opinion, we know Negroes better than anybody else and the integration of competent Negroes and their utilization in the execution of these programs will go far towards helping to solve this problem. I say this not as a Negro, but as an American citizen who is equally as anxious as you to solve this problem.

The Chairman: Is there additional discussion of this progress report? Is there discussion from the Army group or from any of our Canadian neighbors?

Mr. R. F. Voyer (Dallas, Texas): I am a layman in social hygiene and venereal disease control in Texas, but I should like to put before the group a point which I hope will be enlarged upon and discussed by some of you who are far better authorities than I. That is the question as to how the United States Public Health Service, which after all is the instrument under discussion and the instrument which will be used, can utilize the medical profession as a medium for lay education.

It has been my experience in my State that the rank and file of the profession are eager to be used, but they have not been utilized. They lack, unfortunately, by and large the essential knowledge of proper diagnostic and therapeutic procedures, as well as the initiative and the inclination, to spend the time with those whom they diagnose as venereal disease subjects. I should like to hear from some of you, if possible, on this point. Possibly a

resolution can be incorporated in this report which will lend us great aid; the medical profession is the key to this whole problem.

The Chairman: Is there additional discussion along this or other lines?

Dr. James G. Faustina (United States Public Health Service): There is one point in the report that I feel I should react to. Most of my experience in connection with venereal disease education has been in teacher-training institutions, and I am fearful of a recommendation of personal prophylaxis. It has been my experience in working in Negro teacher-training institutions throughout the South and the Southwest that most of the authorities on education are afraid we are going to take the Army approach to the problem, and they are afraid to ask us in for that reason.

I do not feel that prophylaxis is the only answer, and I certainly would have to start again if this committee places too much emphasis in the educational aspect on personal prophylaxis.

I believe that we have thus far considered too much of venereal disease treatment control rather than venereal disease control on the whole. I realize, as Dr. Stokes has mentioned, that if you remove the fear of disease and the fear of unwanted pregnancy from illicit sexual intercourse, there remain only the intangibles of the spirit to restrain an individual. However, it is upon those intangibles of the spirit we in education must concentrate our efforts if we hope to get the full cooperation of the school, the church, and the other community agencies essential for the promotion and success of any program of venereal disease control.

I believe that it should be a basic essential that we proceed on the assumption that self-control is the basis of venereal disease control, especially in our educational programs for the youth in high schools and in teacher-training institutions. We no longer entertain any idea that there is a great possibility of accidental infection in venereal disease. We know that by and large the infections come from sexual intercourse, and with that in mind, we know that these venereal diseases are among the few diseases where it is possible to say that we control the cause. We must have the full cooperation of church groups, community groups, and school groups; this cooperation is necessary and essential to our success.

Frankly, I should like to express a fear of the recommendation of prophylaxis.

In conclusion, I might point out that for a long time an opinion on sex has been in the realm of personal conviction rather than in the realm of natural law. I think that we should take a positive approach to the problem. Instruction that does not result in a change in attitude, that does not result in a willingness and an earnestness to avoid evil, and to choose good must of necessity be somewhat negative. I realize the necessity of reaching teachers in the hope that in so doing the teachers will carry the message to many others whom we cannot reach with a small staff. That is the approach in which I am concerned.

The Chairman: For your information, Dr. Faustina is attached to the Office of Education from the Public Health Service, and is profoundly interested in this question of education in venereal disease control. Is there additional discussion?

Dr. Koch: There is one consideration that to my knowledge has not yet been brought out in this health education meeting, and that is the media of approach that can be used to great advantage, especially in view of the fact that our health educators are few in number. We in San Francisco have experienced considerable success in working with labor unions, in disseminating venereal disease information. Some of you might have seen our exhibit explaining, in a way, the program which we have developed with labor unions. We all know that labor unions are organized on a national basis, and I would like to suggest that the Public Health Service, in addition to the many other recommendations, attempt to formulate a program with such organized groups.

We have, in addition to the labor union movement, the parent-teachers associations that are also organized nationally. If some type of a national program could be outlined which could infiltrate to the local group, it would be very helpful to the local health departments concerned; especially is this true, for example, in the labor unions where it is the members who have venereal disease. Therefore, it is of little value to speak to service organizations like the Kiwanis Club, or the Lions Club, where only a few of the members have venereal disease; they may have had it but they do not have it now.

It is too late. We have to get to people who either have it or potentially will have it.

In addition, one of the further suggestions that could be handled on a national basis is the use of large corporations. I suggest, for example, the Shell Oil Company, the Standard Oil Company, et cetera. We have found marked success in bringing patients to our venereal disease clinics by lavatory signs. In fact, statistics show that 12 percent of our patients who report for examination come as the result of lavatory signs. However, on the local level it is impossible to secure the cooperation of such organizations to place placards in restrooms because it is contrary to their national policy. It seems, for example, that the Public Health Service could do much along this line to facilitate a program that could be established on a local basis following a national program.

The Chairman: Is there additional discussion of this progress report?

Dr. Charles M. Carpenter (Rochester, N. Y.): I am not unmindful of spiritual values, but, on the other hand, I am rather realistic about the question of prophylaxis, and I should like to express an opinion that I have had for sometime. In studying reinfection in patients who have been treated for venereal disease, we find that from 25 to 30 percent are reinfected in from 2 to 8 or 10 months after they have been cured of venereal disease; that indicates that somewhere along the line we are not doing our job. I do not know what the answer is unless it is that we have failed to tell this group of people how they may prevent becoming reinfected. I realize it is a difficult problem, but we should have in every venereal disease clinic what I call a "prophylaxis service," that is, we should teach these people how to prevent getting venereal disease; I might go a little farther and even give these people prophylaxis. If we have to spend money to provide them with free treatment, why not prevent the disease rather than treat it? It would be much less expensive. This may seem like a radical procedure, and I know that it cannot be carried out immediately, but I think that by withholding information from even youngsters in high schools, we are not going to eliminate venereal disease from this country.

The Chairman: Additional discussion is invited of this progress report on matters relative to education, community action, and community control. If not, is the conference ready for the question? It has been moved and seconded that the progress report submitted by Chairman Snow and Dr. Hazen be adopted. Those in favor reply by the usual sign "aye"; opposed. So be it.

[The final report of the Section on Education and Community Action, representing the postconference expansion and revision of the progress report and prepared under the direction of the Section chairman as the formal report of the Section, is published herewith.]

REPORT OF SECTION ON EDUCATION AND COMMUNITY ACTION

Chairman: WILLIAM F. SNOW, M.D.,
Chairman, Executive Committee
American Social Hygiene Association
New York, N. Y.

Secretary: H. H. HAZEN, M.D.,
President, Social Hygiene Society
Washington, D. C.

Four considerations influence the report and recommendations of the Section on Education and Community Action:

1. The family is the basic unit of our society. Syphilis and gonorrhea and the promiscuous sex habits which spread these diseases are a grave threat to the family as an institution, as well as to the public health.

2. The major part of the fight against syphilis and gonorrhea must take place in the community, and must be supported and joined by all important elements of community life. The local health department is responsible primarily for prevention and control of venereal diseases. However, definite responsibility is also borne by local law enforcement, social protection and welfare agencies, the medical and allied professions, and by schools, churches, and civic organizations. The influence of these varied interests and agencies is most efficient when mobilized through a carefully planned program of cooperative community action.

3. To control venereal diseases effectively, influence must be exerted on the attitudes and actions of venereal disease patients, their contacts, and the public. Therefore, education of the patient and of the general public in the nature of these diseases, the modes of transmission, and the necessity for early and adequate diagnosis and treatment is an indispensable part of the prevention and control process.

4. There is urgent need **now** to maintain and increase the fight against the venereal diseases. In addition, psychologic, emotional, and economic problems arising from war and demobilization are likely to create an even greater need in the postwar period.

FAMILY PROTECTION

Since sexual promiscuity is the principal cause of the spread of infection and because protection of the family unit is the concern of all citizens and public officials, the health officer should give utmost support to those agencies and influences which help to develop in members of the family group patterns of conduct which avoid promiscuity.

Education in the home, school, and church which is in harmony with sound social and psychologic principles will be most likely to develop habits and attitudes leading to proper expression of the sex urges. To be most effective, such education must be concerned primarily with improving individual adjustment, strengthening and conserving the family, and improving the community life. Proper facilities for preparing parents and teachers for these educational tasks should be established and supported by States and communities. If necessary, they may be begun as part of long range programs for venereal disease control or general health education. The principles and procedures basic to such education should be developed by qualified professional personnel. Preparation for teaching and consultation should also be made available to practicing and student clergymen.

In addition to their medical and public health aspects, the venereal diseases are "symptoms" suggesting poor sexual behavior, marital maladjustments, psychiatric problems, and in many instances substandard or abnormal economic and environmental conditions for families and children. Thus, in the interests of public welfare and protection of the family unit, many activities not immediately associated with disease control which are performed by social hygiene, mental hygiene, and social welfare agencies need support and expansion.

Summarized briefly, these activities include psychiatric counseling, child welfare and protection, provision of a wholesome environment for youth, sound educational programs reaching adults as well as youth, and the development of a community consciousness of the importance of these and other socially desirable conditions and services essential to healthful and constructive living.

In the field of social welfare work, there are certain minimal services directly related to venereal disease control which should be available. These specific services include social case-work service to or within law enforcement departments, courts, venereal disease clinics, and rapid treatment centers.

Service to or within the police department should include interviewing and referral to appropriate community agencies for treatment and for social services. Services to or within the court should include assistance in the preparation of suitable presentence study following conviction, and competent probation supervision. Services to or within venereal disease clinics and rapid treatment centers should include assistance to patients for the personal or social problems related to illness or medical care and to social redirection or rehabilitation.

MORAL FACTORS

The moral factors inherent in the spread of venereal diseases have received increased attention in recent years. Public health leaders have realized that the extent of the problem and the success or failure of venereal disease control efforts are strongly influenced by standards of sex behavior. The health officer, therefore, has a professional and official interest in the influences which help determine those standards. It is his official duty to support those influences and organizations which seek to reduce promiscuity through ethical and spiritual means for the same reason that it is his recognized official duty to oppose the influences and interests which tend to increase promiscuity.

With the development of safer, faster, and more convenient treatment for syphilis and gonorrhea, an important aspect of cooperation with churches, schools, and parents is to avoid giving the public the false impression that promiscuity has been made safe. Of equal importance is the avoidance of a similarly false impression through the indiscriminate distribution of information about prophylaxis.

It is obvious, however, that sexual morality should not be taught to young people primarily because it serves as a method of avoiding venereal disease infection. Sex promiscuity is only one of many "symptoms" of departure from the moral and ethical principles upon which our culture is based, and venereal disease is only one of the many damaging results of misuse of the reproductive instinct.

As the health officer has an obligation both officially and as a citizen to support those who are responsible for the moral and ethical development of the community, so have the church, the school, and similar institutions an equal obligation to support the community health program. Leaders of church, educational,

parent-teacher, civic, and welfare organizations increasingly realize that, as presented to the public by health authorities, the sober facts of the venereal disease problem and the measures necessary for control provide powerful support for programs aimed at improving the spiritual and social environment. They also recognize that better community health is the concern of all who profess special interest in the total welfare of human beings, and that without good health many spiritual and social values other than good sex behavior are more difficult to attain.

This commonalty of interests dictates close cooperation between medical and public health forces and the leaders of religious, educational, and character-building groups. More study and evaluation of the various means for developing this cooperation is needed, and will be undertaken by other committees.

VENEREAL DISEASES AND SOCIAL HYGIENE EDUCATION

All people need accurate information about the venereal diseases appropriate to their age and cultural status. The information to be given the general public regarding the extent of the problem and the medical measures for control should be provided by the health authorities, the medical profession, and responsible research agencies. As an indication of what can be accomplished through consistent education of the public, physicians, health departments, and special groups, the Section calls attention to the steady decline in the reported incidence of congenital syphilis observable in many areas, and to the virtual disappearance of gonorrheal ophthalmia.

The effective telling of these facts is not only the prerogative of official health authorities, but also an essential part of their responsibility for providing leadership and stimulus to the whole program of cooperative action at local, State, regional, and Federal levels.

Active use of the various channels of public information and education is important. The press and radio, motion pictures, posters, literature, lectures, and discussion groups all should be used to the fullest extent possible in accordance with the scope of the problem and the particular educational needs of the community. All people of the community must be reached with this information in such a number as to provide motivation and public approval for specific action. In carrying out this phase of his responsibility with efficiency, the health officer will often need the assistance of voluntary or paid health educators and information specialists.

To carry out at the national level responsibility for securing the informed citizenry whose support and cooperation are essential in eradicating the venereal diseases, the United States Public Health Service should provide ample funds for an active health educational program, including preparation of materials to be used in State and local programs, and provision of expert advisory services in health education and community organization. Federal provision should also be made for research in the most effective educational methods and materials, including evaluation and demonstrations. The Public Health Service should also serve as a clearing house for the interchange of ideas, pro-

grams, and materials between the various State and local educational programs, and should maintain close contact with the health authorities of other nations in this particular aspect of venereal disease control so as to aid the prevention of international spread of infection.

It is important that similar provision be made by State and local health departments for the effective conduct of venereal disease education, including purchase or production of materials, use of qualified personnel, and the provision of demonstration and consultative services to cooperating official and unofficial agencies.

Patient education.—Medical officers in charge of venereal disease clinics or rapid treatment centers, and private physicians have a professional obligation to provide venereal disease patients with the basic facts about these diseases, how they are contracted, diagnosed, and treated, and how they may be avoided and prevented from spreading.

It is believed that the all-important contact-tracing phase of organized venereal disease control, as well as the prevention of reinfection of patients, will be greatly facilitated by realistic and intelligently applied patient education. To carry out this education in clinics and rapid treatment centers, it is essential that all staff members coming into contact with patients or suspects be thoroughly trained in the essential facts of venereal disease diagnosis, treatment, epidemiology, prevention, the importance of patient education, and the methods by which it may be achieved.

For instruction of patients and other persons who have not had the benefit of or obviously will not respond to ethical, moral, or intellectual teachings, physicians, clinics, and rapid treatment centers have an obligation to impart the scientific facts regarding personal prophylaxis. The Joint Prophylaxis Committee report of the Public Health Service and the American Social Hygiene Association is approved by this Section as a detailed statement on this problem and on prophylaxis procedures.

Education in schools.—It is recognized that in recent years the secondary school has had to assume much of the nonacademic teaching and character training formerly supplied in the home. Principles of personal and social conduct are formed by many youths on the basis of their school experiences. Obviously, it has become necessary to include in the schools in many communities instruction in personal ethics and conduct. Since promiscuity and venereal disease are dangerous to the family, teachings of the character generally described under the headings "Preparation for Family Life," "Health and Human Relations," "Social Hygiene," et cetera, should be included in the formal curriculum. It is strongly recommended that this instruction be conducted only by teachers who have had adequate training, and who have the appropriate qualifications in personality and experience. The activities of Federal and State health departments, boards of education, and colleges in providing teacher-training courses, institutes, and workshops are commended and their expansion is urged.

It is also strongly recommended that general health education be conducted in schools, including instruction in personal hygiene, public health and sanitation, the structure and physiology of the human body, and information about the communicable diseases.

This Section strongly condemns the practice in many schools of omitting the human reproductive processes from the study of physiology and biology, and elimination of venereal diseases from the study of communicable diseases. Also condemned is the common practice of confining venereal disease and sex hygiene instruction to the occasional brief and usually rather furtive and abrupt "lecture" by a visiting physician or nurse, with no opportunity for competent advice or consultation following such lectures. It is believed this short-sighted type of education is more harmful than beneficial to many students.

The Section on Education and Community Action is of the opinion that up to the present time the public health aspects of the venereal diseases have been insufficiently taught in the medical schools of the United States, and it is urged upon those responsible for the arrangement of the curriculums to correct this deficiency. The Section is of the same opinion regarding the training of public health nurses and social workers.

COMMUNITY ORGANIZATION AND ACTION

In order to bring about the public action necessary to develop and maintain effective local conditions and practices in support of the medical control program, communities must often be mobilized and organized. There are, of course, organizations present and already at work in many communities whose objectives are synonymous with or directly related to venereal disease control. Social hygiene societies, social protection committees, wartime health councils, councils of social agencies, and various specialized health associations are examples. But in many areas there are no such groups; sometimes even when they are present they may be ineffective or unwilling to cooperate. It becomes of paramount importance, then, that State health departments, the United States Public Health Service, the Social Protection Division of the Federal Security Agency, and the American Social Hygiene Association cooperatively promote organization in those communities where organization is lacking and where the problem is severe.

The Section on Education and Community Action recommends the practice of stimulating laymen to study all types of health problems for the purpose of developing organized methods for their solution, often leading to the creation of a lay community health council. This may be city- or county-wide in scope depending on the nature of the area; it may direct its efforts toward improving all types of local health conditions, bearing in mind, however, the urgency and importance of the venereal disease problem, and the practical program for eradication which has now been demonstrated. Where there are several health groups already present, they may wish to form a council to serve as a coordinating as well as a promotional body. Often a community war council or a similar civic coordinating body already exists and may be persuaded to consider health and venereal disease control measures as an integrated function of the organization.

In the absence of these facilities, the following procedure is recommended:

1. Under the auspices of one or more responsible public or private civic bodies, call together a group composed of designated

representatives of city and/or county commissioners, bar association, medical society, chief of police, county sheriff, city and/or county health department, board of education, chamber of commerce, merchant's league, service club, ministerial associations, interracial committee, welfare association, labor group, parent-teacher groups, voluntary health agencies, social hygiene societies, social protection committees, and similar groups which have some professional or community interest in the field. The facts of local health conditions should be presented and thoroughly discussed, the group asked to plan for solution of the problem. This often leads to the appointment of a steering committee and the selection of a number of influential and public-spirited citizens and officials to serve as a board of directors responsible for drawing up a comprehensive tentative plan. A small executive committee should be chosen and a chairman elected from among the members of this group to meet with various appropriate officials to draft the program, this should be put in writing. Assistance in this drafting process usually can be had from the State or local venereal disease control officer, health educator, and social protection or social hygiene representatives.

2. Usually, it has been found helpful to encourage interim interest and activity of the members of the board of directors by designating several sections, each with a capable and influential specialist serving as chairman in charge. Sections on law enforcement, social welfare, health education and information, medical services, and group participation are usually included.

3. It is recommended that each section be responsible for its share of the total program, and that day-to-day activities be coordinated through an executive secretary responsible to the executive committee of the board. Where possible, this secretary should be a full-time employee, experienced in community organization work, and thoroughly familiar with the community and its problems.

4. No community action campaign is successful in the long run unless it reaches and motivates the average man. It is his health with which we are concerned and his cooperation obviously should be secured. Education alone will not suffice; active public participation is required.

5. Because the venereal diseases are closely tied up with personal habits and emotional adjustments, the mental hygiene aspects of a control program should not be overlooked. It is recommended, therefore, that preventive mental hygiene and corrective personal guidance activity be specifically included in the program of the community committee, probably under the supervision of the social welfare section.

The value of the generalized health approach, particularly from the long range viewpoint, lies in the greater likelihood that citizen interest and participation can be elicited and maintained, and in the administrative soundness of such procedure. There is a minimum of emotional or prejudicial opposition. Venereal disease, as one of the urgent community problems of our time, must receive its full share of attention from the whole community.

Negro participation.—Because of limited economic, social, and educational opportunities and other conditions which have aided

the spread of the venereal diseases widely among members of their race, Negro leaders are most anxious to cooperate actively in national, State, and local control efforts. In many areas, some of the most effective preventive and educational work has been accomplished principally because of this cooperation. Therefore, it is recommended that particular attention be given to securing full participation from responsible Negro leaders in all phases of community organization for venereal disease control.

Long range programs for social hygiene and venereal disease education in schools and clinics in areas having a sizable Negro population should make full use of qualified Negro professional and community workers, and provide special training for Negro teachers. In the production or purchase of educational materials, Federal, State, and local health departments and other interested organizations both official and voluntary should include posters, pamphlets, and visual materials especially designed for the basis of the experience and requests of these qualified workers.

Other special groups.—It is recognized that in addition to the patients of private physicians, clinics, and rapid treatment centers there are many other groups of youths and adults which should be reached through education as a factor in case finding, case holding, and prevention of exposure. Of particular importance are persons who are separated from the normal influences of an established home, family and friends, recreational facilities, and other environmental safeguards. In their search for recreation and friendship many of these persons, particularly those who have not had the benefit of appropriate teaching and training in self-control in their childhood and early youth, are likely to become exposed and infected by venereal disease. This likelihood, however, could be reduced through realistic and vigorous education pointing out the possible consequences of promiscuity, suggestions for less dangerous and more satisfying types of activity, symptoms of infection, and the need and availability of diagnostic and treatment measures. There will remain certain individuals who cannot or will not avoid exposure but will profit by prophylaxis instruction, and every appropriate means should be employed to inform them.

PREVENTION OF PROSTITUTION AND PROMISCUITY

In 1941, the Federal Government established, as an integral part of the program for wartime venereal disease control, a Social Protection Division in the Federal Security Agency, to be responsible for implementing point 6 of the Eight-Point Agreement adopted by the Army, Navy, Public Health Service, and the Conference of State and Territorial Health Officers. Point 6 established an official Federal and State policy for prostitution repression as a measure necessary to effective venereal disease control. It defined responsibility and promised cooperation in the following words: "The local police department is responsible for the repression of commercialized and clandestine prostitution. The local health departments, the State Health Department, the Public Health Service, the Army, and the Navy will cooperate with the local police authorities in repressing prostitution." Under the general coordination of the Social Protection Division, red-light dis-

tricts have been closed in more than 650 communities throughout the United States. Wherever the repression of organized prostitution was effective, infection rates declined in nearby Army and Navy establishments.

In spite of the success of law enforcement in wiping out organized prostitution, there are indications that advocates of the segregated districts and those who profit from the prostitution racket are awaiting relaxation of wartime controls with full plans for a return to "business as usual." The Section therefore urges Federal, State, and local governments and responsible citizens everywhere to oppose this threat with every resource.

Experience gained during the present war supplements previous demonstrations that an effective social protection program on an organized, official basis can provide invaluable assistance to venereal disease control, and that it should include the following major functions:

1. Enforcement of all laws which relate to the repression of prostitution and promiscuity.
2. Stimulation of public interest in and support for adequate medical and social services and facilities.
3. Development of individualized social services for those persons participating in unlawful sex practices, and in cooperation with health and medical authorities for those undergoing medical treatment for venereal diseases.

To carry out those functions on a coordinated Nation-wide scale, representatives of the Federal Government should cooperate with the States and their communities, placing technical experience and skill at the disposal of the State and local health, law enforcement, and welfare agencies. This Section of the conference recommends the continuance of social protection facilities and qualified personnel for fully coordinated Federal, State, and community programs.

The sociologic problems of prostitution and sexual promiscuity are exceedingly complex. They are fostered by economic forces which decree that the ability to earn an independent existence shall precede marriage; thus legitimate sexual relationships are delayed beyond the age of sexual competence and desire. These problems are made more acute by feeble-mindedness, sex precociousness, poor home environment, lack of recreational and community services, and by many other undesirable conditions, all of which are aggravated in time of war and of postwar reconstruction.

The ultimate solution of the prostitution problem involves the fields of economics, sociology, and human relations. It must be determined what causes girls and women to become prostitutes, and preventive measures should be applied before they become habitual sex offenders. A society which continues to neglect the basic causes of prostitution or to protect those who are incapable of protecting themselves is as "antisocial" as the prostitute and her patrons.

Prevention of sexual promiscuity.—The war impact upon communities, with its accompanying disorganization of family life, laxity in moral restraints, and emotional hysteria is partly responsible for the increasing number of venereal disease cases at-

tributed to the promiscuous amateur. Mothers and fathers are often absent from their homes and lose their influence over their sons and daughters. In addition to this freedom from parental restraint, often there is freedom from financial restraint since young girls and boys are able to command good salaries in war plants and other jobs. Unfortunately, they do not often know how to use this freedom. The result is reflected in widespread juvenile delinquency and an increase in sex delinquency among young people.

The home, the school, the church, and the community at large are responsible for this situation, and should not permit conditions to exist which lead to the doors of the courtroom or venereal disease clinic.

Functions of law enforcement agencies.—The success of police action in the repression of prostitution, and the apprehension and detention of people connected with prostitution, sexual promiscuity, and related misdemeanors depends largely upon the correct definition of the function of law enforcement, and the extent to which workable and sound relationships are established with the health and welfare agencies of the community.

Legislation.—In this connection, it must be reiterated continually that law enforcement officers can work only within the framework of the criminal law, as differentiated from protective health and social welfare laws, rules, and regulations. Law enforcement officers should not arrest, hold or detain women and girls simply because they "suspect them of having a venereal disease." Nor should law enforcement officers be used as "contact-tracers" by the health department. Only after the health department has exhausted its resources for locating or interviewing persons suspected of being infected with venereal disease should it furnish the law enforcement officer with a health warrant or quarantine order so that the person may be detained for examination. Under our legal code, it is no crime to be infected or suspected of being infected with a venereal disease; also the discovery that a person who has been arrested is not infected does not justify dropping the charge.

Persons arrested on morals charges should be examined for venereal disease infection. In the case of juveniles, such an examination should never be made without the explicit permission of the child's parents.

The success of police action depends upon cooperation from the courts, but the courts' hands are tied without adequate legislation. Offering advisory services for the preparation and submission of appropriate legislation is one of the functions of an official social protection or a voluntary social hygiene agency. State health laws for venereal disease control and laws against prostitution and allied activities should be revived, amended, or initiated where needed. Injunction and abatement laws under which houses of prostitution may be closed should be strengthened and enforced. Preventive legislation, such as laws specifying wages, hours, and types of employment for girls under 18 years of age, licensing laws prohibiting the sale of liquor to minors, drunken persons, etc., along with local ordinances for "protective" services, all come within the purview of social protection.

Courts.—The presence or absence of venereal disease is not a factor to be considered in the determination of innocence or guilt by the court. What the court does with persons apprehended, taken into protective custody, or tried for a criminal offense is, however, definitely of importance to social protection and venereal disease control. Offenders against antiprostitution or promiscuity laws should, if possible, be given the kind of sentence, probation, or case-work service which will be most helpful in keeping them from returning to the activities which brought them to the attention of the court.

After a person is judged guilty or not guilty, the court should withhold sentence until a study has been made of the health, personality, and social background of the offender. This presentence study helps the court determine what would be the best method of making provision for the readjustment of the individual from the standpoint of his or her welfare, as well as that of society.

Medical treatment in relation to courts.—If a person who is infected is sentenced to a jail, reformatory, or prison, provision should be made for treatment during confinement. Courts should not commit infected persons to rapid treatment centers. No person should be held in any rapid treatment center under bond, penal restraint, or court order. However, if probation is granted and faithful attention to treatment is made one of the conditions of probation, experience has shown that it is practicable for a rapid treatment center, venereal disease clinic, or private physician to cooperate with the court authorities by furnishing medical treatment.

Detention facilities.—Increased attention should be given to the provision of safe, sanitary, and humane detention facilities for all persons arrested on charges related to prostitution. Juveniles should not be detained in jail and every effort should be made to return the child to his home. If the juvenile is a runaway from out of town, has no home, or if it is not considered advisable to send him home, every effort should be made to find a suitable place, other than the jail, where he may stay while awaiting the action of the court. Younger persons should be separated from older and confirmed offenders. Persons with communicable diseases should be separated from well persons, and a matron should be in attendance wherever female offenders are detained.

Functions of health agencies in relation to social protection.—While the diagnosis and medical treatment of the venereal diseases are the responsibility of professional medical practice, the elimination of the venereal diseases demands the practical use of all resources—nonmedical as well as medical.

Health departments have within their authority both the power and responsibility for bringing under medical treatment all persons known or suspected of having any infectious venereal disease.

The health department should inform the police department of places to which the spread of venereal disease has been traced, and request appropriate investigation and action against the offending establishments and persons (including hotels, taverns, taxicabs, and tourist camps). Similarly, health departments are responsible for furnishing information to the courts as to the

existence and circumstance of known infections in order to assist the courts in making proper disposition of offenders.

Function of social services.—At no time should it be forgotten that prostitutes, promiscuous persons, and those who are infected with venereal diseases are human beings with complex feelings, motives, and habits. Thus, in dealing with those who come in contact with the authorities (whether medical, correctional, preventive, or rehabilitative) these factors must be taken into account. Services should be made available to these people in keeping with their needs and in a manner which they can accept.

Public and private welfare agencies have made a beginning in assuming responsibility for this type of service. A clear delineation of the social service function is necessary so that it does not interfere with nor assume police or health functions.

The function of social case work is to help the individual to utilize his potentialities for handling difficulties within his own individual situation. The case-work services of public and voluntary agencies can be of valuable assistance to the police in dealing with young people against whom there is no charge, and who have not been arrested. Referrals for this type of service are usually most effective when there is a policewoman or juvenile aid bureau within the police department. The appropriate social agencies should make their services available both day and night; they should use initiative in dealing with the individuals brought to their attention, and should be prepared to deal with unusual situations with great flexibility.

Many patients coming to venereal disease clinics or rapid treatment centers can profit from case-work treatment as well as medical care. Experience has shown that such service under these conditions can be most effectively carried out through medical social services, provided by the responsible health authority operating the clinic or center. Both public and private welfare agencies should help patients before they enter the rapid treatment centers to solve such problems as care for children, arrangements with employers, travel to the rapid treatment center, clothing, et cetera, so that medical treatment will not be complicated unduly by personal problems. Case-work services for social diagnosis and referral should be provided in the rapid treatment centers. Services of public and private agencies should be available in the community to those patients who want help with their problems upon discharge from the centers.

The courts should have probation departments which are responsible for making presentence studies and for rehabilitative services. However, in the absence of a probation staff, the court may request the services of qualified voluntary agencies in making social, psychiatric, and psychometric studies of the offender after determination of guilt and prior to sentence. When there is no probation department, the court may request the voluntary agency to accept the offender on probation. Confidential material developed in the course of such supervision cannot be given to the court except with the permission of the client.

Social case work should be available within correctional institutions as integral parts of the rehabilitation program.

Current problems in social protection.—The social protection activities of the Federal, State, and local governments now face a critical period. The gains made against commercialized prostitution must be held and further advances made in the war against sexual promiscuity. The weapons of law enforcement, social services, and medical treatment must be used wisely and vigorously. The community, the school, the church, the home must be enlisted in the battle. It must be realized that there will be, eventually, an end to booming war industries and the armed conflicts in Europe and Asia, but that venereal diseases, prostitution, and allied antisocial influences will not automatically disappear with the cessation of hostilities. On the contrary, World War I and other experiences indicate that there is grave danger of a general letdown in repression, prevention, and control measures.

In the years to come, when the military forces and personnel in training and industrial employees and our families in homes all need protection, it will be necessary to continue support of the principles of the "Eight Point Agreement," amended and applied to meet peacetime conditions. The essential philosophies and relationships set forth to implement this agreement by the Army, the Navy, the Public Health Service, the State and Territorial health departments, the Federal Security Agency, and the American Social Hygiene Association will be needed during the period of reconversion, and afterwards.

The May Act (Public Law 163, passed by Congress in 1941) makes engaging in, or aiding and abetting, prostitution, a Federal offense in areas designated by the Secretary of War or the Navy. It has proved itself to be a strategic reserve force for aiding and supplementing local powers and authority. It should be extended beyond its present expiration date, May 15, 1945, and amended in such ways as may increase its usefulness.

The Chairman: This concludes the business session of the conference, but before adjournment I should like to express on behalf of the Public Health Service, and personally, very sincere thanks to our gracious hosts of St. Louis, those who made our stay so very pleasant, and especially to the St. Louis Medical Society for the use of this lovely building and for the much appreciated services of Miss Patton, the Assistant Secretary, who has been untiring in her efforts to make our stay pleasant and to make the conference run as smoothly as it has. I should like for Miss Patton to say a few words.

Miss Patton: Thank you very much. On behalf of our society I should like to say that we have been very glad to have you. We are proud of our building and are glad to have visitors. This has been one of the most splendid and one of the largest meetings we have ever had in the building.

Dr. Clarke (New York): May I offer a resolution? I move that the National Conference on Postwar Venereal Disease Control express its thanks to the St. Louis Medical Society for its hospitality in making its splendid facilities available for the purpose of this conference. We also express our appreciation for the services of Dr. Edwin Ernst, President of the St. Louis Medical Society, in planning the housing of this conference, and of the staff of the Medical Society in aiding us to conduct a satisfactory series of meetings.

The Chairman: There is a resolution before the house. I should like a second to this resolution.

[The resolution was seconded.]

The Chairman: It has been moved and seconded. I will ask for a vote. Those in favor of incorporating reply by the usual sign "aye"; opposed. It

is so ordered. It will be incorporated and copies will be sent to the appropriate officials.

I should like to thank again, on behalf of the Public Health Service, and personally, the chairmen and secretaries of the sections who have been so very helpful to the conference in getting together material for the subsequent study and guidance. I should also like to thank the participants on the program, those who delivered such splendid papers and otherwise contributed so much, and of course all of you who came and gave so generously of your time, and very precious professional time it is. It has been a very great pleasure for us to have you here, and we trust that while we hope we do not have more venereal disease control war conferences and few, if any, additional venereal disease control conferences, if we do they will be even better conferences than this one, which is the best I, personally, have attended.

Dr. Charles E. Miner (Atlanta, Ga.): I cannot resist, just as a member of the conference, the opportunity to say that I think all of us from our places on the floor ought to say to you that we appreciate the dignity and high character with which you conducted the chairmanship of this conference.

[The Conference adjourned officially at 3:20 o'clock.]

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AUTOPSY STUDIES IN SYPHILIS

A Monograph by

PAUL D. ROSAHN, M. D.

No. 21

From the Department of Pathology, Yale University School of Medicine, and the Laboratories of the New Britain (Connecticut) General Hospital

Aided by a grant from the Venereal Disease Division of the United States Public Health Service.

FEDERAL SECURITY AGENCY

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THOMAS PARRAN, *Surgeon General*

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Dedicated to the Memory

of

WADE H. BROWN, M. D.

(1878–1942)

ACKNOWLEDGMENT

In April 1940, the writer solicited the financial support of the United States Public Health Service for a study of syphilis at autopsy to be based on the Yale post-mortem protocols. The proposal received the warm approval of Dr. R. A. Vonderlehr, then Chief of the Venereal Disease Division, and later of his successor, Dr. J. R. Heller, Jr., to both of whom grateful appreciation is extended. Their encouragement and critical judgment were of inestimable assistance in the development of the project.

By rare good fortune Dr. Bernard Black-Schaffer became associated with the investigation soon after its inception. He brought an active mind, great enthusiasm, and untiring effort to the task, until larger opportunities attracted him in 1942 to the Medical College of Virginia and more recently to Duke University. Dr. Black-Schaffer shared authorship in most of the publications arising from this study. It was largely due to his inexhaustible efforts that the laborious task of coding the autopsy protocols was completed.

The results of this investigation were published in several scattered reports under the general title "Studies in Syphilis." These papers are here collected under one cover. They originally appeared in the Archives of Internal Medicine, the American Journal of Syphilis, Gonorrhea and Venereal Diseases, the Yale Journal of Biology and Medicine, and the Journal of Venereal Disease Information. It is a pleasure to record thanks and appreciation to the editors and publishers of these journals for reprint permission.

The original texts are not here faithfully reproduced in meticulous detail. Rather, modifications, addenda, and deletions have been introduced wherever indicated. These, however, in no respect alter the basic tenets of the study as originally conceived and published.

November 1, 1946 PAUL D. ROSAHN, M. D.

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INTRODUCTION [1]

linical investigations of the biology of yhilitic infection have been directed essen- iy to the problems of diagnosis, therapy r its complications, end results, and serol- g. By its very nature, the clinical approach e been practically limited to the study of h disease in the viable host, and as a result ny tangential issues have received no more n cursory and scattered attention. It is ap- ent that the coordination and correlation he clinical aspects of the disease with the lervations at autopsy will throw light on ny problems which are still in the penum- of knowledge. How frequently do persons n clinically diagnosed syphilis present rphologic evidence of syphilis at autopsy? hat is the relationship between clinical cure morphologic lesions at death? How often s a person with clinically diagnosed hilis die as a direct result of his disease, how often is the disease a contributory n noncontributory factor in causing death? the distribution of the causes of death ong persons with syphilis, apart from this ase, any different from that of the non- hilitic population? Of corollary interest, s syphilis confer any susceptibility or re- ance to other diseases? What, for instance, he probability of death from cancer or m other morbid processes among syphilitic compared with nonsyphilitic persons? Is re any correlation between serologic obser- ions and morphologic evidence of syphilis death? How does the longevity of the hilitic person compare with that of the nsyphilitic?

A stimulating paper by Moore (*1*) tersely nmarized many unknowns in syphilology. "In spite of 400 years of study, we still do not know the actual importance of syphilis as a cause of death . . . To what extent . . . does death directly from syphilis masquerade under other diagnoses; or to what extent is syphilis an indirect cause of death from other conditions? . . .

"The modern necropsy studies of syphilitic patients, such as those of Warthin, provide no answers to these questions. Such studies, while revealing a very high incidence of lesions of syphilis, especially in aorta, heart, meninges, and testes, provide no correlation between the clinical status and the necropsy findings, no information as to cause of death, and no data as to the kind and amount of treatment, if any, given during life. What is clearly needed is a detailed study of both clinical and necropsy data in a very large series of patients, to provide information as to the frequency with which patients recognized as syphilitic during life, either on clinical or laboratory grounds, showed lesions of syphilis at necropsy and what these lesions, if any, were; the frequency with which patients adequately studied during life with no discoverable evidence of syphilis showed such evidence at necropsy; the relationship of clinically or pathologically recognized syphilis to the final illness and the direct or indirect cause of death; the relationship of necropsy evidence of syphilis to treatment during life; and a dozen similar factors as yet unknown."

These and other related problems form the background for a survey summarized in the following pages. The basis for this study consists of 5,300 autopsies performed in the Department of Pathology at the Yale University School of Medicine since 1917. Supplementary and complementary information has been derived from a review of the pertinent literature.

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is and the following chapter revise the article *dies in Syphilis. I. Review of the Incidence of hilis in Autopsies on Adults,* by Paul D. Rosahn Bernard Black-Schaffer, which was published in *Archives of Internal Medicine,* vol. 72, p. 78, 3.

REVIEW OF THE INCIDENCE OF SYPHILIS IN AUTOPSIES ON ADULTS

The literature on the pathologic changes of syphilis contains no comparative or summated analysis of the isolated surveys of autopsy populations that have appeared from time to time. Many authors have directed their attention to specific types of syphilitic lesions, and as a result the scope of their studies has been limited to particular organ systems or to special tissue reactions. Comparatively few investigators have been concerned with the incidence of syphilis at autopsy in its broadest, all-inclusive aspects, and many of their studies have appeared in foreign publications not readily accessible in the United States.

It is here the principal purpose to collate and evaluate the available reports on the frequency of morphologically diagnosed syphilis in autopsy populations. The review is concerned with syphilis in its acquired form, and for convenience in analysis the autopsy populations have been limited to persons aged 20 and over. Wherever necessary, published reports have been recast to give the incidence of syphilis by decades beginning with the age of 20. This revision, however, in no way alters the factual data presented by the authors. It is admitted at the outset that there may be included a certain small number of syphilitic persons over 20 with congenital infections, but these are adequately counterbalanced by the exclusion of persons under 20, some of whom no doubt had acquired syphilis. At any rate the populations under consideration are large enough to reduce effectively any error introduced by taking the age of 20 as the arbitrary lower limit of acquired syphilis.

The Incidence of Syphilis at Autopsy

Table 1 presents a summary of ava reports on the incidence of syphilitic le in autopsy populations. The data of this are graphically depicted in chart 1. countries of continental Europe, one in one West Indian island, and the U States are represented. The frequenc syphilitic changes encountered at au among persons over 20 years of age from a low of 2.6 percent to a high of percent. The average for all of the 17 re presented in the table is 8.8 percent. average, however, gives equal weight to of the reports regardless of the numb observations on which it was based. An native average value is one based or entire summated autopsy population ir 17 reported series. Of a total of 146,761 sons, 7,993, or 5.45 percent, were obs to be syphilitic at autopsy.

Other reports on the incidence of syph lesions at autopsy are available, but fo stated reasons they were not incorporat table 1. Brines (*2*) studied 618 ro autopsies performed in 1934 at the Ci Detroit Receiving Hospital, where 36 pe of the patients admitted were Negroes found 54 instances of gross and micros syphilis, an incidence of 8.7 percent, failed to give the age and sex compositi the autopsy group. Turnbull (*3*) st more than 7,000 necropsies performe London between 1908 and 1913 and f that approximately 4 percent had lesio acquired syphilis. Incomplete data preve exact computation of incidence. Pohlen reviewed 8,182 autopsies performed in deburg between 1928 and 1936. Of the

TABLE 1.—*Incidence of syphilis at autopsy among persons aged 20 and over*

Author [1]	Country	Years	Number of autopsies	Persons with syphilis	
				Number	Percent
H[illegible]heimer [2]	Germany	1906–1930	10,300	270	2.60
B[illegible] (10)	U. S. A.	1910–1937	19,785	601	3.04
G[illegible]rich [3]	Germany	1914–1924	23,179	806	3.48
H[illegible]steen [4]	Norway	1907–1925	11,376	515	4.53
T[illegible]ori (17)	Italy	1918–1935	7,673	371	4.84
F[illegible]s (18)	Italy	1928–1933	8,217	418	5.09
M[illegible]hior (19)	Denmark	1914–1920	4,594	245	5.33
L[illegible]ger [5]	Germany	1906–1925	23,015	1,268	5.51
G[illegible]lberg (23)	Norway	1896–1930	8,235	481	5.84
S[illegible]mers (11)	U. S. A.	1906–1916	5,000	314	6.28
N[illegible]el (21)	Germany	1907–1933	11,476	827	7.21
O[illegible]n (12)	U. S. A.	1931–1938	5,408	418	7.73
O[illegible]ls (7)	U. S. A.	1900–1923	2,492	280	11.24
K[illegible]isch (9)	Puerto Rico	1926–1938	665	75	11.28
M[illegible]har (8)	India	1927–1934	2,721	431	15.84
H[illegible] (6)	U. S. A.	1922	850	179	21.06
W[illegible]hin (5)	U. S. A.	1909–1929	1,675	494	29.49
Total (7 different countries)		1896–1938	146,761	7,993	5.45

[1] Figures in parentheses refer to bibliographic references.

[2] Herxheimer, J.: Syphilitische Veränderungen des Herzens und der Arterien, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 16, pt. 2.

[3] Gürich: Ueber die syphilitischen Organveränderungen die unter dem Sektionsmaterial der Jahre, 1914–1924, angetroffen wurden, Münchn. med. Wchnschr. 72:980, 1925.

[4] Hansteen, cited by Guldberg (22).

[5] Langer, E.: Die Häufigkeit der luetischen Organveränderungen, insbesondere der Aortitis luetica, München med. Wchnschr. 73:1782, 1926.

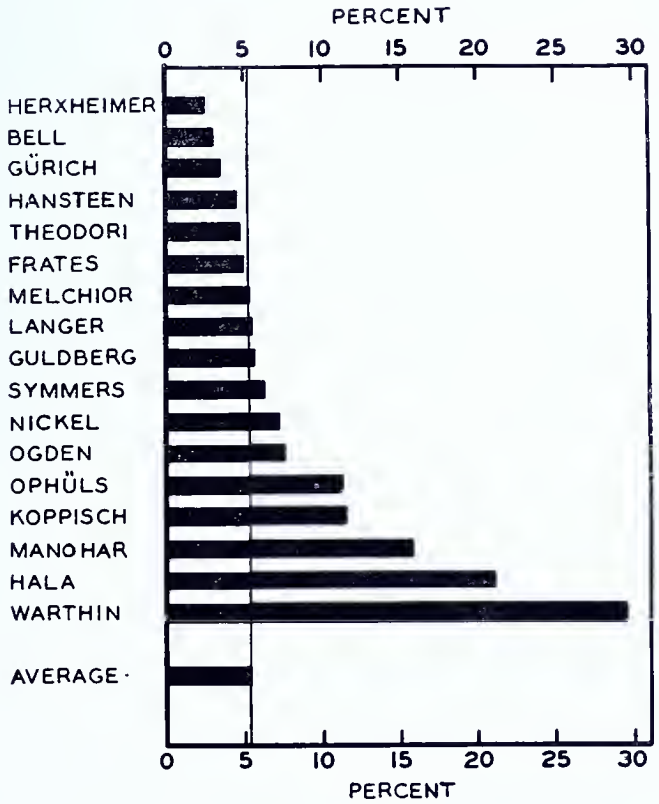

CHART 1.—The incidence of syphilis at autopsy among individuals over 20 years of age.

jects studied, 557, or 6.8 percent, had morphologic evidence of syphilis. This value includes both those with congenital and those with acquired lesions, who cannot be readily segregated on the basis of the data as given.

Twelve of the 17 reports listed in table 1 showed an incidence of syphilis of less than 8 percent, and only 5 authors gave an incidence higher than 11 percent. A comparison of individual results shows a striking variation between those of Warthin (*5*), Hala (*6*), Ophüls (*7*), Manohar (*8*), and Koppisch (*9*), on the one hand, and the remaining authors on the other. If we place the summated observations of these 5 authors in one classification and compare their results with those of the remaining authors, the difference is striking:

Authors	*Autopsies* *Number*	*Instances of syphilis* *Number*	*Percent*
Warthin, Hala, Ophüls, Manohar, and Koppisch	8,403	1,459	17.36
12 Others	138,358	6,534	4.72

It is, moreover, apparent that as regards reports emanating from the United States, there are two clear-cut and distinct schools of opinion. The first school, represented by Bell (*10*), Symmers (*11*), and Ogden (*12*), reported 1,333 instances of syphilis among 30,193 autopsies on persons aged 20 and over, a frequency of 4.4 percent. Warthin (*5*), Hala (*6*), and Ophüls (*7*) representing the second school, found 953 cases of syphilis in an autopsy population of 5,017, an incidence of 19 percent. The marked disparity between these two sets of results represents one of the outstanding problems of modern syphilology.

It is conceivable that the differences are real and characteristic of the different populations under investigation. On this basis syphilis was actually ten times as frequent in the population studied by Warthin as in that surveyed by Bell. If it is true that treatment effectively eliminates all morphologic traces of syphilis, the variable incidence might be explained by differences in the availability and intensity of syphilotherapy in the several communities forming the reservoirs for the different autopsy populations. Information on this point is outside the range of the present report, but other siderations suggest that the entire explan does not lie in this direction. In the place, the primary premise, that treat effectively eradicates the morphologic ch of syphilis, is a problem yet to be se In the second place, even if this pr were accepted, the necessary conclusion syphilis is treated over four times more tively in New York, where Symmers f an incidence of 6.3 percent, than in igan, where Warthin reported a 29.5 p frequency, would appear untenable.

Other factors, such as variability in nomic status, in race, in age, and in distribution of the subjects comprising different autopsy populations, are of in tance, and these will be discussed in s quent paragraphs. A critical analysis o diagnostic criteria employed by the dif authors may also throw some light on widely divergent findings.

Analysis of Variables Contribu to Differences in Incidence

Race

It is well known that syphilis is more frequent in the American Negro in the white race. Keidel and Moore among 5,000 patients admitted to the ical ward of Johns Hopkins Hospital, positive Wassermann reactions of the in 7.6 percent of the white persons a 22.9 percent of the Negroes. Among discharged medical patients, syphilis w agnosed in 9.7 percent of the white pe and in 25.4 percent of the Negroes.

An excellent opportunity to evaluate differences in the frequency of syphilit fection was afforded by the data accumu under the provisions of the Selective T ing and Service Act of 1940. Vonderleh Usilton (*14*) analyzed the serologic bloo reports received through August 31, 19 1,895,778 white and Negro men be ages 21 and 35. The rate of prevalen syphilis, based on positive and dou blood tests, was 252.3 per thousand a Negro selectees, as contrasted to 17.4 thousand among white selectees.

Other authors, notably Turner (*15*) Paullin, Davison, and Wood (*16*), hav

rted comparable results. However, it is not ssible to explain the divergent results sumarized in table 1 entirely on the basis of e racial composition of the different topsy populations. All the European paents were adult Caucasians, and this is true so of Warthin's group. The population udied by Ophüls was composed of 91.3 pernt white persons; no attempt was made to rrelate race with morphologic changes, beuse of the small number of Negroes. Hala nd Symmers made no mention of the racial mposition of their groups. In Koppisch's ries the incidence of syphilis among white ersons was 8.6 percent, as contrasted to an cidence among mulattoes of 13.8 percent nd among Negroes of 16.9 percent. These st two groups comprised 37.5 percent of the opulation and contributed 52 percent of the yphilitic subjects. The relatively high incience of syphilis reported by Koppisch can us be accounted for at least in part by the nclusion of a large number of mulattoes and Negroes, in whom the disease is more frequent than in the white race. Ogden's autopsy roup consisted of 2,280 white persons, 89 f whom had syphilis, an incidence of 4 ercent, and 3,128 Negroes, 329 of whom ad anatomic syphilis, an incidence of 10.5 ercent. Manohar's observations will receive ore detailed discussion later.

The cardinal point with regard to race is hat, although syphilis is demonstrably more requent in the Negro than in the white person, the racial composition of the different populations is alone insufficient to explain the diverse results. Warthin, reporting the highest incidence, studied a population consisting solely of white persons.

Manohar requires special consideration because he was dealing with natives of India, a racial group not comparable to any investigated by the European and American authors. His series consists of two groups. The first was composed of 882 persons autopsied at the Grant Medical School, in Bombay. Syphilis was diagnosed at autopsy in 20.7 percent of these. The second comprised 1,839 persons autopsied by police surgeons, among whom 13.1 percent had lesions of syphilis. In the latter group only the principal cause of death was investigated, while the first was thoroughly studied by complete gross examinations. This author recorded the remarkable observation that 49 percent of the persons autopsied at the Medical School had syphilitic lesions of the heart, generally recognizable on gross examination. This observation, which is at complete variance with the entire literature, is explicable only on the basis of the author's diagnostic criteria. These, however, he fails to describe.

Social and Economic Status

It is difficult to evaluate the social and economic status of the autopsy populations studied by the various authors listed in table 1. Most of the reports are based on persons in the general category "city hospital patients." There were private patients in the series studied by Bell and in the populations analyzed by several of the German and Scandinavian authors. From this viewpoint alone, the 29.5-percent incidence of syphilis in Warthin's group of "private patients" is noteworthy.

Sex

Only five of the authors named in table 1 have published sufficient information to relate sex to acquired syphilis demonstrable by lesions at autopsy. Their reports are summarized in tables 2 and 3. Of 40,934 autopsied persons over 20, 62.3 percent were men and 37.7 percent were women. Among these, 1,763 had evidence of syphilitic infection, of whom 75.4 percent were men and 24.6 percent were women. Whereas approximately three-fifths of the autopsy population were men, men accounted for three-fourths of the cases of syphilis. Analysis by the chi-square test of homogeneity (table 3) indicates a statistically significant difference between these values. It can be concluded that a higher proportion of men and a lower proportion of women showed evidence of syphilis at autopsy than could be expected on the basis of the proportions of the sexes in the combined populations. Syphilis was diagnosed in 5.2 percent of the male population, a significantly higher percentage than that observed among women, i. e., 2.8 percent.

Each of the five authors presenting data on the sex incidence of syphilis at autopsy reported a frequency among males approximately twice that observed among females.

TABLE 2.—*Frequency of syphilitic lesions in men and in women as diagnosed at autopsy by five different investigators*

Author	Number of autopsies	Men, total		Women, total		Persons with syphilis			
						Men		Women	
		Number	Percent	Number	Percent	Number	Percent	Number	Percen
Bell	19,785	13,103	66.2	6,682	33.8	480	3.6	121	1
Frates	8,217	5,217	63.5	3,000	36.5	314	6.0	104	3
Koppisch	665	494	74.3	171	25.7	65	13.2	10	5
Melchior	4,594	2,482	54.0	2,112	46.0	171	6.9	74	3
Teodori	7,673	4,222	55.0	3,451	45.0	300	7.1	124	3
Total	40,934	25,518	62.3	15,416	37.7	1,330	5.2	433	2

Unfortunately, the reports of four authors, namely, Ophüls, Manohar, Hala, and Warthin, who found the highest incidence of syphilis, do not lend themselves to an analysis of the sex distribution either of their total autopsy population or of their syphilitic population. A critical evaluation of their material in the light of this general conclusion with regard to sex is therefore not feasible. It is, however, justifiable to conclude that the varied incidence of syphilis encountered by the different observers cannot be wholly the result of a preponderance of males in their autopsy populations.

TABLE 3.—*Frequency of syphilitic lesions in men and in women as diagnosed by five different investigators (observed and expected values)*

[Summarized from table 2]

Sex	Syphilitic		Nonsyphilitic		Total
	Observed	Expected	Observed	Expected	
Men	1,330	1,099	24,188	24,419	25,518
Women	433	664	14,983	14,752	15,416
Total	1,763	1,763	39,171	39,171	40,934

Age

The data presented by Teodori (*17*), Bell (*10*), Frates (*18*), Melchior (*19*), and Koppisch (*9*) are the only published reports sufficiently exhaustive to permit of a summated analysis of the incidence of syphilitic lesions at autopsy in relation to age at death. The findings of these five authors form the basis for the following discussion of age and syphilis in men at autopsy. The last author's data are not included in the consideration of age and syphilis in women because of the small number of women in his series. The data are presented in table 4 and in charts 2, 3, and 4. The figures were drawn on arithmetical probability paper and show the cumulative pe centages by decades. A normal frequency di tribution when charted on this type of pap is represented by a straight line. Deviatic from a straight line is indicative of corr sponding deviation from a normal distrib tion. The median is easily determined grap ically by the intersection of the 50-perce ordinate with the frequency curve. The slo of the frequency line indicates the degree variability of the data: the steeper the slop the greater the variability (Schrek (*20*)).

The mean age (chart 4) of nonsyphili men over 20 was 54.70 ± 0.14 years, value significantly higher than that found f nonsyphilitic women, 52.09 ± 0.23 yea The mean age of the men with syphilis w 52.53 ± 0.36 years, which is significant

TABLE 4.—*Analysis of sex distribution persons with and without syphilitic lesio at autopsy*

Age	Nonsyphilitic			Syphilitic		
	Number	Percent of total	Cumulative percent	Number	Percent of total	Cum lati perc
	MEN [1]					
20–29	2,229	9.2	9.2	22	1.7	1
30–39	2,356	9.7	18.9	173	13.4	15
40–49	4,459	18.4	37.4	358	27.7	42
50–59	5,373	22.2	59.6	381	29.5	72
60–69	5,384	22.3	81.9	272	21.1	93
70+	4,391	18.2	100.0	86	6.7	100
Total	24,192	100.0	.....	1,292	100.0	...
	WOMEN [2]					
20–29	2,191	14.8	14.8	21	5.3	5
30–39	2,297	15.5	30.2	62	15.5	20
40–49	2,384	16.1	46.3	95	23.8	44
50–59	2,383	16.1	62.3	106	26.5	71
60–69	2,716	18.3	80.6	80	20.0	91
70+	2,874	19.4	100.0	36	9.0	100
Total	14,845	100.0	.....	400	100.0	...

[1] The data are based on the reports of Bell, Frates, Koppis Melchior, and Teodori.

[2] The data are based on the reports of Bell, Frates, Melch and Teodori.

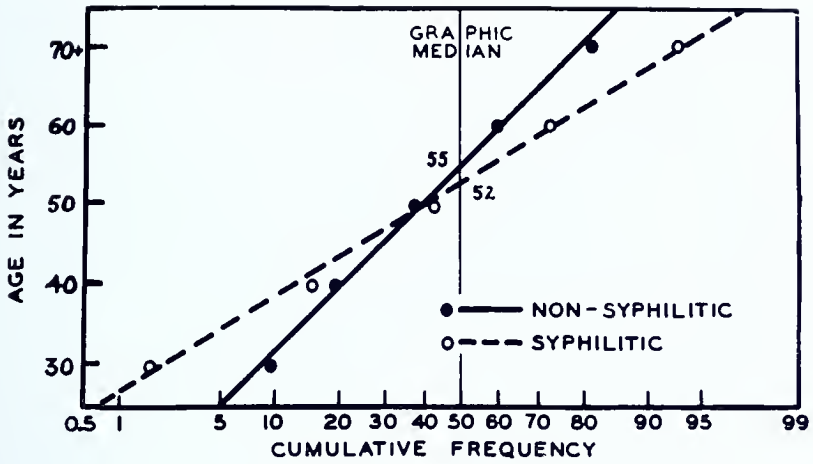

CHART 2.—Age of males with and without syphilitic lesions at autopsy.

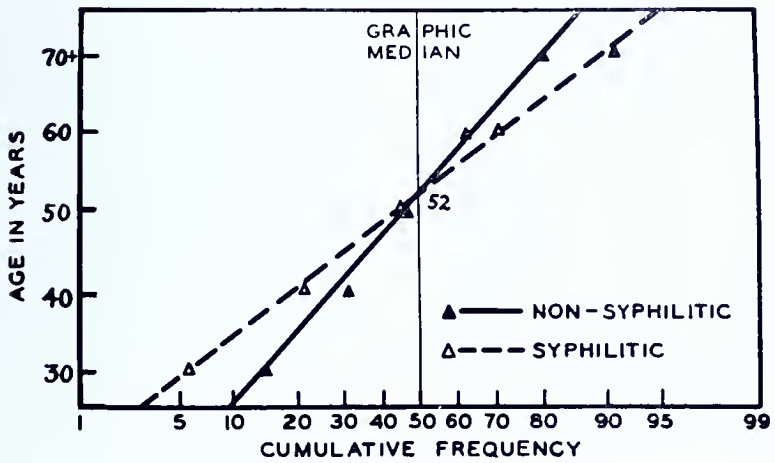

CHART 3.—Age of females with and without syphilitic lesions at autopsy.

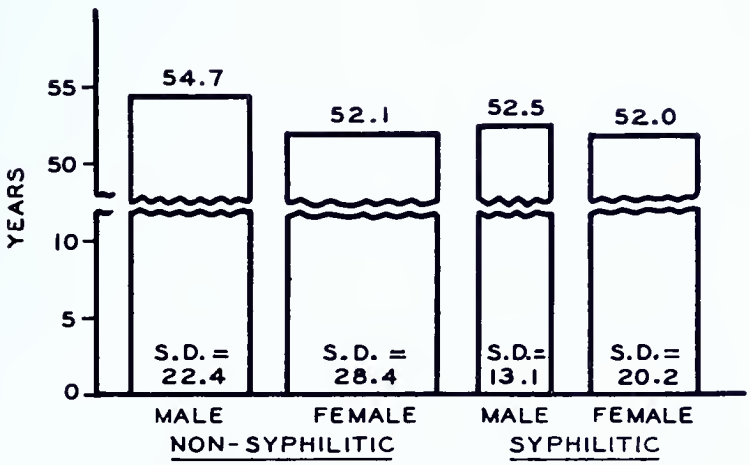

CHART 4.—Mean age and standard deviation of male and female individuals with and without lesions of syphilis at autopsy.

lower than that of the nonsyphilitic men. In contrast to this finding, the mean age of syphilitic women was 51.95 ± 1.01 years, actually no different from the mean value for the nonsyphilitic women. In these cumulative observations it appears that the average span of life of the syphilitic man was shortened by about 2 years, as compared with that of the nonsyphilitic man, although the woman with syphilis had an average duration of life no shorter than her nonsyphilitic sister. Differences in sex apparently exerted no significant influence on the average age at death of the syphilitic person, since both men and women with syphilis had a mean age of about 52 years.

Great care must be exercised in drawing conclusions from the mean age at death, because such values are easily affected by variations in the age distribution of different groups. For this reason the analysis shown in table 4 and charts 2 and 3 is presented. About 9 percent of the deaths in the nonsyphilitic male population over 20 years of age occurred during the third decade of life, as compared with less than 2 percent of the deaths among syphilitic men. Approximately 50 percent of the deaths in the nonsyphilitic group occurred between 30 and 59 years of age, while 70 percent of the syphilitic deaths took place in this age class. Finally, about 20 percent of the nonsyphilitic men survived beyond the age of 70, in contrast to less than 7 percent of those with syphilis.

A similar analysis of the data for women gives essentially similar results. About 15 percent of the deaths among nonsyphilitic women took place in the third decade of life, as compared with only 5 percent of the syphilitic deaths. Approximately half of the nonsyphilitic women died between 30 and 60 years of age, as compared with two-thirds of the syphilitic women. Moreover, about 20 percent of the nonsyphilitic women survived beyond the age of 70, in contrast to only 9 percent of the syphilitic women.

It is not our intent that these curves be interpreted as being typical of syphilis in this country. A composite curve was drawn instead of individual curves for each author in order to smooth the irregularities that would appear in the limited observations in the individual reports. These composite curves should be compared with each o as regards syphilitic and nonsyphilitic sons. From this viewpoint, and in the c bined experience of the authors cited, syphilitic man living into the forties and syphilitic woman living into the fifties h shorter life span than their nonsyphi brother and sister. It should be noted each of the curves in charts 2 and 3 is re sented by a straight line, indicating a no frequency distribution. In chapter 5 t findings will be compared with those of Yale experience, and the close parallelism tween the two series will be shown.

One other observation with regard to is of significance. This refers to the degre variability of the frequency distributions the syphilitic and nonsyphilitic men women. In charts 2 and 3 the slope of curve indicates variability; the steeper slope the greater the variability. In cha variability is proportional to the width of bars. In both sexes the age distribution of syphilitic group is less variable than tha the nonsyphilitic group, and this differenc highly significant. (The standard devia equals 22.4 ± 0.10 for nonsyphilitic and 13.07 ± 0.27 for syphilitic men, difference being 9.33 ± 0.27, and t,35. standard deviation equals 28.4 ± 0.16 nonsyphilitic women, and 20.2 ± 0.23 syphilitic women, the difference being 8.2 0.28, and t,30.) The extremes of age betw 20 and 70 are lopped off in the syphi groups as compared with the nonsyphil Fewer young and fewer old subjects found in the syphilitic than in the syphilitic population.

The incidence of syphilis diagnosed autopsy in relation to age and sex is sh in table 5. The highest incidence of syp occurred among men in the fifth decade among women in the sixth decade, but each decade syphilis was more frequ among men than among women. A poss but completely improbable explanation the high incidence of syphilis in Warthi Hala's, and Ophüls' populations is here i cated. If their autopsy populations were c posed entirely of Negro men aged 40 to a plausible explanation for the high i dence of syphilis which they reported mi be offered. There is internal evidence in t

publications, however, to discredit this hypothesis, and other explanations must therefore be sought.

TABLE 5.—*Incidence of syphilitic lesions at autopsy in men and in women according to age, by decades*

[Summated from reports of Bell, Frates, Koppisch, Melchior and Teodori]

Age	Total number		Syphilitic persons			
			Number		Percent	
	Men	Women	Men	Women	Men	Women
20-29.....	2,251	2,212	22	21	0.98	0.94
30-39.....	2,529	2,359	173	62	6.84	2.62
40-49.....	4,817	2,479	358	95	7.43	3.83
50-59.....	5,754	2,489	381	106	6.62	4.26
60-69.....	5,656	2,796	272	80	4.80	2.86
70-.....	4,477	2,910	86	36	1.92	1.24
Total...	25,484	15,245	1,292	400	5.07	2.62

Diagnostic Criteria

It is generally recognized that the criteria for the pathologic diagnosis of syphilis are not definitive. Before the advent of Warthin's *The New Pathology of Syphilis* a relative uniformity of criteria did not exist. These criteria were and still are to be found in the standard textbooks here and abroad. Outside of the United States and Canada, Warthin's influence has failed to make the impression which, on this continent at any rate, has resulted in the broadening of the pathologic concept of syphilis. This influence is more readily appreciated when the reports on lesions of individual organs, such as the stomach, testicle, kidney, liver, and adrenal glands, are considered than when the more general reports, such as those of table 1, are reviewed. It must, however, be stated that before Warthin's publications appeared, the specific nature of the syphilitic lesion was the object of much controversy and in fact was the very basis which made Warthin's interpretation possible.

Because of the paucity of comparable anatomic studies, and the total lack of uniformity of criteria, the entire subject of the pathology of syphilis is a maze in which both the expert and the not-so-expert are frequently lost. When the incidence of syphilis of the liver in comparable populations ranges from 3.3 percent to 33.4 percent and when one author designates all hepatic syphilis as hepar lobatum, while another diagnoses only 33 percent as such, it is obvious that complete confusion in terminology and interpretation of lesions exists. It thus becomes apparent that of primary importance in an evaluation of statistics of this type are the criteria followed by the different observers. Here one finds sufficient variability to account in large part for the divergent results.

Warthin (*5*) stated: "The pathologic diagnosis of syphilis is essentially microscopic. Only in a relatively small number of cases are the gross lesions . . . typical enough to be recognized by the naked eye. A negative diagnosis of syphilis cannot be given with any certainty without a routine microscopic examination of all organs and tissues, but particularly of the left ventricular wall, the aorta, both its arch and abdominal portion, the testes, pancreas and adrenals . . .

"The new pathology of syphilis is based upon the demonstration that the essential tissue lesion of either late or latent syphilis is an irritative or inflammatory process, usually mild in degree, characterized by lymphocytic and plasma cell infiltrations in the stroma particularly about the blood vessels and lymphatics, slight tissue proliferation, eventually fibrosis, and atrophy or degeneration of the parenchyma."

This concept is in direct contrast to that of Nickel (*21*), who is representative of many of the authors listed in table 1. Nickel's criteria may be freely translated as follows: "Only definite anatomic syphilis, i. e., syphilitic vascular disease, syphilis of the central nervous system, syphilis of the bone, gumma, and interstitial hepatitis of the newborn, was included. Presumptive evidence of syphilis was not considered, i. e., orchitis fibrosa, cicatricial atrophy of the tongue, and so-called syphilitic cirrhosis, nor was a positive Wassermann reaction." Nickel specifically disregarded orchitis fibrosa, lingua glabia, and so-called syphilitic cirrhosis of the liver, nor did he mention changes in the pancreas and adrenals, as did Warthin. The latter also emphasized testicular fibrosis, and, in fact, Weller (*22*), who was for many years associated with Warthin, made the following statement: "In our opinion, testicular lesions rank second only to those of the aorta as to value in recognition of latent (nongummatous) visceral syphilis." The contrast between Warthin and Nickel is readily apparent and

is so sharply drawn that their conclusions cannot be fairly compared.

Symmers employed essentially the same criteria as Nickel but differed from him in the interpretation of specific lesions. For example, Symmers found that 33.4 percent of his syphilitic subjects presented hepatic syphilis of both the hepar lobatum type and the cirrhotic form, while Nickel specifically excluded from his series subjects with so-called syphilitic cirrhosis. Moreover, Symmers included subjects with the "presumptive changes of syphilis," such as orchitis fibrosa and lingua glabia, in his series. In spite of this, it is noteworthy that there is no significant difference between the 7-percent incidence reported by Nickel and the 6 percent observed by Symmers.

Hala, apparently a disciple of Warthin, accepted as syphilitic any subject to whom two of the following criteria applied: (1) a clinical history of antecedent infection or clinical evidence of existing syphilis, (2) a positive Wassermann reaction, (3) the observation of typical gross lesions at autopsy, and (4) histologic evidence of syphilis.

It is evident that the first two criteria are not anatomic, and since the number of subjects admitted to the series on this basis is not stated, the comparative value of the entire work is placed in jeopardy. Moreover, the freedom which the four criteria give to the author is evidenced by the statement that "subpleural aggregations of small round cells (miliary gummata?)" were noted in a considerable number of persons with syphilis, all of whom had pulmonary tuberculosis and the large majority of whom died of tuberculosis.

Frates included not only persons with anatomic lesions but also those with a positive Wassermann reaction or a clinical history of infection. However, these two groups are so well differentiated that it was possible to recalculate the author's findings and incorporate in table 1 only those cases in which there were definite anatomic lesions of syphilis.

Although Ophüls did not enumerate criteria in a formal statement, one may deduce them from his paper. For example, he included a subject with "myocardial syphilis on the basis of clinical history and course." He included another with chronic diffuse interstitial inflammation of pulmonary tissue cor pulmonale, designated as syphi Twenty percent of Ophüls' syphilitic pat had syphilitic hepatic disease, in contra Warthin's 30 percent and Nickel's 4.23 cent. Ophüls also included patients orchitis fibrosa but added, "They ma syphilitic." The remainder of the authors lowed in general the criteria describe Nickel.

The reports show considerable vari with respect to the routine use of m scopic examination of tissues, or of examination alone, in the anatomic diag of syphilis. There is, however, compe evidence that this variation is less impo in accounting for the difference in frequ rates than is the variability in diagn criteria. Among authors relying entirel almost entirely on gross examinatio reaching a diagnosis of syphilis are Teo Frates, Symmers, Manohar, and Ophüls. first three reported a frequency of 4.8 cent, 5.1 percent, and 6.3 percent, re tively. These are all comparable results. last two authors recorded rates two and t times as great, that is, 15.8 percent and percent. It appears from these reports there is distinct lack of uniformity in th terpretation of the gross tissue changes duced by syphilis.

The same variability in diagnostic cri is apparent in the reports based on m scopic evidence of syphilis. These include reports of Guldberg (23) (5.8 perce Koppisch (11.3 percent), Hala (21.1 cent), and Warthin (29.5 percent). The of these authors found no greater incide syphilis through the study of routine h logic preparations than did Teodori, Fr or Symmers, all of whom relied pred nantly on gross examination alone. The parity between Guldberg's observations the one hand, and Warthin's, on the o is so striking as to suggest that it results so much from a real difference in the dence of syphilis in the two populatio from significant differences in the diagn criteria followed by the two investigators

The conclusion is warranted that the a clear need for a restatement of the mor logic changes, both gross and microsc which result from syphilitic infection. Th especially true with regard to the histo

erations described by Warthin as definite, and this aspect of the problem will be discussed in a subsequent chapter. Precise evaluation of the anatomic changes of syphilis in terms of morbidity and mortality will depend primarily on the standardization of diagnostic criteria and on the general adoption of a uniform nomenclature.

MATERIAL AND METHODS OF ANALYSIS OF YALE AUTOPSY PROTOCOLS[1]

The previous chapter was devoted to a review of the literature on the frequency of the changes attributed to acquired syphilis in autopsies on individuals over 20 years of age. It was found that syphilitic changes observed at autopsy by 17 different reporters varied from a low incidence of 2.6 percent to a high of 29.5 percent with a combined average of 5.45 percent among 146,761 autopsied adults. A critical analysis of the wide discrepancies between the observations of different investigators was made, and it was concluded that the differences resulted largely because of the great variability in the criteria employed in arriving at a gross or microscopic diagnosis of syphilis.

Subsequent sections will be based primarily upon a study of the autopsies performed at the Yale University School of Medicine, together with supplemental information from the literature. This chapter will describe this material and discuss the methods employed in analyzing it. The punch-card code finally adopted for the survey is presented in the appendix. In addition, two samples from the nonsyphilitic population will be compared with each other and with the residue of the nonsyphilitic population with respect to age, sex, and race. It will be shown that these two groups represent a random selection from the total nonsyphilitic population in our autopsy series, and therefore can be used as standard nonsyphilitic controls for comparison with the syphilitic group.

Source of Autopsy Population

The material available for examination and analysis consists of the hospital records, autopsy protocols, and microscopic sections 5,300 consecutive autopsies performed at Yale University School of Medicine in period from September 22, 1917, to March 1941. These necropsies were conducted various prosectors affiliated with the Depa ment of Pathology during this period. T largest proportion of subjects were refer for necropsy by the New Haven Hospi which is a nonprofit association serv primarily the city and county of N Haven, but receiving patients also fr other communities in the State and oc sionally from outside the State. In 19 4,529 patients were admitted. During course of the next 24 years, the capacity creased to 524 beds in 1941, and 12,6 patients were admitted during the fiscal y 1940-41. Of the 524 beds, 330 were served for ward patients, 88 for semipriv patients, and 106 for private patients. Fr September 1917 to July 1940 a total 9,162 admitted patients of both sexes and all ages died. Of this number, 4,371, or percent, were autopsied, and 69 percent these autopsies were upon individuals ag 20 years or more.

The city of New Haven, in which most the patients entering the New Haven H pital reside, is a manufacturing and univ sity community whose inhabitants are larg Caucasian, numbering approximately 162,0 The population has been fairly constant this level during the last 20 years, foreig born whites comprising approximately percent. In the census of 1940 there w 6,235 Negroes—about 4 percent of the to population.

The 5,300 consecutive autopsies no above included 3,907 necropsies on indiv uals of both sexes aged 20 years and ov Of these, 3,187 died at the New Hav Hospital and 96 at the affiliated Willi

[1]This chapter and the appendix are revisions of the article *Studies in Syphilis. II. Methods of Analysis of Yale Autopsy Protocols,* by Bernard Black-Schaffer and Paul D. Rosahn, which was published in the *Yale Journal of Biology and Medicine,* vol. 15, p. 575, 1943.

irt Winchester Tuberculosis Hospital. An ditional 438 died at State tuberculosis nitoriums, at other hospitals, or at home, d 186 were coroner's cases where death curred before admission to the New Haven ospital.

Selection of Syphilitic Group

The complexity of analyzing a large topsy population by the old hand method f sorting and tabulating is at once appar-nt. The punch-card system of analysis lends self conveniently to this type of survey and as therefore adopted. Rosahn (*24*), in 938, described the application of the Hol-rith punch-card system to the analysis of utopsy protocols, and the first 4,000 autop-ies in this series represent the same cases oded by him in 1938. The additional 1,300 ases which brought the total to 5,300 were oded and punched according to the manner escribed by Rosahn in his original communi-ation. These 5,300 cards were sorted ac-ording to age, and 1,393 autopsies on pa-ients under 20 years of age were eliminated. As indicated previously, age 20 has been aken arbitrarily as the lower age limit of cquired syphilis. It is recognized that this procedure may result in the inclusion of a small number of syphilitic individuals whose nfection is of congenital origin, but these are counterbalanced by excluding persons under 20, some of whom may have the lesions of acquired syphilis.

The remaining 3,907 cards representing individuals aged 20 or more were then sorted for syphilitics and for suspected syphilitics. The criteria employed in choosing these cases were as follows: (1) A past history of primary or secondary infection or a positive serologic reaction; (2) a history of anti-syphilitic therapy; (3) a positive serologic reaction during the last admission or significant findings in the spinal fluid; (4) a clinical diagnosis of syphilis; (5) a positive serologic reaction at post-mortem; (6) an anatomic diagnosis consistent with syphilis. The clinical charts for all cases meeting any one of the above criteria were obtained wherever possible, and critically evaluated. In addition, the clinical records of all patients with a known family history of syphilis were also studied. A total of 380 cases diagnosed as syphilitic on clinical or laboratory or post-mortem evidence remained, and this group hereinafter will be referred to as the "experimental" or "syphilitic" group. It should be noted at this point that 380 out of 3,907 adults in our series, or 9.7 percent, presented a clinical history consistent with a diagnosis of syphilis, or findings at autopsy consistent with such a diagnosis, or both. This represents the aggregate incidence of syphilis in our adult autopsy population and will receive further comment.

Selection of Control Group

In order to facilitate comparisons between the experimental group and nonsyphilitics, 2 control groups of nonsyphilitics were established, each of which contained the same number of individuals as the experimental group. The purpose of selecting 2 control groups was to test each against the other as regards race, sex, and age distribution in order to verify the method devised for random sampling. This method consisted in arranging each of the 380 cards comprising the experimental group in sequential order by autopsy number and similarly arranging each of the remaining 3,527 cards representing the total nonsyphilitic population. The first group of controls hereinafter designated as "control group A" was selected by taking the first card in the nonsyphilitic series following each card for a syphilitic, and the second control group, hereinafter designated "control group B," was similarly derived by segregating from the nonsyphilitic population the fifth card following that for each syphilitic. In this way 2 control groups were established having the same temporal distribution in our autopsy series as the syphilitic group.

Comparison of Control Groups with Total Nonsyphilitic Population

To establish the reliability of control groups A and B as random samples from the total nonsyphilitic population, they were classified as to sex, race (white and non-white), and age.

Sex

There were 226 males (59.5 $\pm$ 2.52 percent) among the 380 individuals in control

group A; 238 males (62.6 ± 2.48 percent) among the 380 in control group B; and 2,232 males (63.3 ± 0.81 percent) among the 3,527 individuals comprising the entire nonsyphilitic population. No significant differences exist among these values and it can be concluded that as regards sex the 2 control groups represent a random selection from the nonsyphilitic autopsy population.

Race

Control group A had 363 white individuals or 95.53 ± 1.06 percent of the total in the group; control group B had 358 white persons or 94.21 ± 1.20 percent of the total; and the total nonsyphilitic population of 3,527 had 3,314 whites or 93.96 ± 0.39 percent. The remaining individuals were Negroes, with one exception, an Oriental. The differences among these values are statistically nonsignificant, so that the 3 groups are homogeneous as regards color.

Age

The decennial age distribution of white and nonwhite males and females comprising control groups A and B and the residue of the nonsyphilitic population is shown in tables 6 and 7. No significant differences were encountered by applying the chi-square test of homogeneity. (White males: Chi-square = 11.66, N = 12, P = 0.476, not significant. White females: Chi-square = 13.09, N = 12, P = 0.369, not significant. Nonwhite males: Chi-square = 0.56, N = 4, P = 0.966, not significant. Nonwhite females: Chi-square = 2.71, N = 4, P = 0.611, not significant.) So far as age is concerned the control groups represent a random selection from the total nonsyphilitic population.

The above analysis indicates that with gard to sex, race, and age the two cont groups can be used as representative of total nonsyphilitic population in mak comparisons with the experimental gro This method of comparison will be u wherever necessary in subsequent chapters

Code for the Study of Syphilis

Following the selection of the syphil and control groups, a new code was drawn with the object of extracting as much p tinent information as possible concern syphilis and related states. Wherever t were available, the clinical records of th three groups were obtained and the requi information derived from them. Moreov the autopsy protocols were re-examined a the tissues were subjected to further mic scopic study. The code as finally utilized pears in the appendix, and using this co new cards were punched for the syph group and for the two control groups. coding diagnoses the *Standard Nomenclat of Disease* classification was employed, w minor modifications to conform to the stu

TABLE 7.—*Age and sex distribution of n syphilitic nonwhite individuals in Yale autopsy series*

Group	Sex	20–39 years	40–59 years	60+ years	Total	A u kn
Control A	Male	3	5	2	10	
	Female	1	5	1	7	
Control B	Male	4	4	2	10	
	Female	4	4	3	11	
Residue	Male	37	40	24	101	
	Female	25	26	19	70	
Total	Male	44	49	28	121	
	Female	30	35	23	88	
Total		74	84	51	209	

¶1 1 Oriental.

TABLE 6.—*Age and sex distribution of nonsyphilitic white individuals in Yale autopsy series*

Group	Sex	20–29 years	30–39 years	40–49 years	50–59 years	60–69 years	70–79 years	80+ years	Total	Age unkno
Control A	Male	24	29	36	47	33	31	11	211	
	Female	7	26	24	31	28	20	8	144	
Control B	Male	23	28	38	58	47	23	7	224	
	Female	17	16	18	28	22	18	10	129	
Residue	Male	156	170	346	359	342	193	68	1,634	
	Female	128	142	148	185	180	104	39	926	
Total	Male	203	227	420	464	422	247	86	2,069	
	Female	152	184	190	244	230	142	57	1,199	
Total		355	411	610	708	652	389	143	3,268	

FIBROSIS AND ROUND CELL INFILTRATION OF THE PARENCHYMATOUS ORGANS (WARTHIN) IN THE TISSUE DIAGNOSIS OF SYPHILIS [1]

In chapter 2 evidence from autopsy studies by different investigators has been cited which indicates the wide variability in the incidence of tissue changes attributed to syphilitic infection. The frequency of morphologic evidence of syphilis among individuals aged 20 and over ranges, according to different reporters, between the extremes of 2.6 and 29.5 percent. Analysis of our own material gave an incidence of 4.0 percent. Certain variables which might have contributed to the widely different incidence rates were critically reviewed, and it was concluded that the lack of uniform criteria for the tissue diagnosis of syphilis was the most important factor involved. The highest rates were reported by investigators who followed the criteria defined by Warthin (5), while those reporting the lowest incidence either antedated Warthin or did not adopt his teachings.

The Warthin Lesion

Warthin's original description (5) of the lesion which he interpreted as indicating syphilitic infection follows:

Heart.—The heart in every case showed microscopic lesions characteristic of spirochete localization . . . The cardiac lesions in the cases in which syphilitic infection was known to exist, and in those in which it was not suspected are identical. They vary greatly in degree . . . It must be emphasized that the determination of cardiac syphilis is essentially microscopic . . .

The essential lesion of cardiac syphilis is an interstitial myocarditis characterized by infiltrations of lymphocytes and plasma cells along the vessels between the muscle fibers. These infiltrations are usually patchy or diffuse, very rarely focal or circumscribed . . . The infiltrations vary in degree, but usually are slight, the cells often being arranged in close single file between the fibers . . . The cells of the infiltrations are probably chiefly histogenetic lymphocytes and young formative cells. Large epithelioid fibroblasts are very common, especially in the older, healing areas . . .

. . . In the most severe cases larger areas of infiltrations are grouped around the coronary arterioles. These may reach such a size as to suggest miliary gummata . . .

. . . In the older healed areas the stroma becomes fibroid and hyaline. In the great majority of cases the myocardium shows healed, fibroid areas in association with the active infiltrations. In many cases the fibroid areas predominate and search may be necessary to show the presence of active infiltrations. This is true especially of the older unrecognized cases. In every case, however, such active areas have been found, and no completely healed cases have been seen. A progressive fibrosis of the myocardium always takes place. In acquired syphilis the fibroid areas are always larger on the endocardial side; but in some cases they have extended completely through the myocardium . . . These marked changes practically always occur just above the apex, in the anterior wall of the left ventricle: . . . The 'fibroid' heart is the ultimate outcome of all cases of latent syphilis.

Pancreas.—The pancreas in all of the old cases of syphilis showed a greater or less degree of atrophy and interstitial fibrosis. In the majority of cases the changes were irregularly scattered throughout the organ, the body and the tail portions showing an especial tendency to involvement. Lobules showing marked change may be surrounded by those showing no change. In other cases the entire pancreas showed a diffuse fibrosis, varying from slight to the most marked degree. The connective tissue increase is both inter- and intralobular. In the majority of cases it was old, containing few cells . . . Careful search has revealed, however, in every case active

[1] This chapter revises the article *Studies in Syphilis. V. An Evaluation of Fibrosis and Round Cell Infiltration of the Parenchymatous Organs (Warthin) in the Tissue Diagnosis of Syphilis,* by Paul D. Rosahn and Bernard Black-Schaffer, which was published in the *American Journal of Syphilis, Gonorrhea & Venereal Diseases,* vol. 28, p. 142, 1944.

areas of plasma-cell infiltration. These areas often show an edematous or myxomatous connective tissue, the plasma-cells and lymphocytes may be few or many . . .

As to the syphilitic nature of these lesions, they are identical with those produced by the spirochete in other tissues and organs. The localized plasma-cell infiltrations, slight fibroblastic proliferation, edematous or mucoid stroma eventually fibrosis, are histologically specific characteristics, I believe . . .

Adrenals.—Small infiltrations of plasma-cells and lymphocytes are of constant occurrence in the adrenals of cases having known syphilis and unsuspected latent syphilis. In the great majority of cases these infiltrations are slight. They occur usually in the medullary portion or in the inner portion of the reticular zone of the cortex. They are usually perivascular. Fibroblastic proliferation of the stroma or fibrosis may or may not be present; the capsule of the organ is usually thickened, and perivascular infiltrations of small size occur in the surrounding tissues. The walls of the blood vessels usually are thickened . . .

Liver.—The liver showed chronic passive congestion and atrophy (brown atrophy chiefly) in every case. Gummata were found in 5 cases, hepar lobatum in 8, atrophic cirrhosis in 10 and an intralobular cirrhosis in 1, Glissonian cirrhosis in 3 cases, while localized fibrosis was very common. The inflammatory lesions varied from slight plasma-cell infiltrations of the periportal tissue to the most marked cirrhotic changes. The relationship of these latter changes to syphilis has not been absolutely determined except in a few cases in which spirochetes were found in such infiltrations . . .

Testis.—In all of the male cases the testes showed varying degrees of atrophy and fibrosis. In the more active cases plasma-cell and lymphocyte infiltration between the tubules, fibroblastic proliferation of the stroma, thickening of the basement membrane and diminished spermatogenesis are the chief changes. These changes may involve the entire organ, or occur in small scattered patches. In the older cases the germinal epithelium of the tubules may be entirely lost, the tubules collapsed, and represented entirely by the hyaline-thickened basement membrane . . . The interstitial cells remain preserved, and in many cases appear hypertrophic. The stroma between the tubules is thickened and hyaline. In severe cases the entire testis becomes fibroid . . .

It is common knowledge that most American pathologists have not accepted Warthin's concept of the tissue changes described in detail above. Nevertheless, a few pathologists have adopted his criteria, and this has led many clinicians to conclude that questionab syphilitic lesions such as chronic syphilit myocarditis, syphilitic gastric ulcer, and di fuse syphilitic hepatitis are well-establishe pathologic entities. In the many years th have elapsed since Warthin's original pape no organized systematic investigation h been made to verify the point of view h espoused. In the present chapter an attemp will be made to evaluate Warthin's dic for the diagnosis of syphilis of the paren chymatous organs, through the use of recog nized statistical technics.

Material and Methods

The analysis is based on a comparisc of the incidence of fibrosis and round ce infiltration (hereafter termed the "Warthi lesion" in the interest of brevity) in th parenchymatous organs of 2 populations. Th first group, described in chapter 3, consis of 380 syphilitics, so diagnosed by historica clinical, laboratory, or post-mortem evidenc They were selected from among 3,907 autop sies on persons aged 20 years or over, pe formed at the Yale University Departme of Pathology from 1917 to 1941. The secon group is the residue of 3,527 nonsyphilit persons in the series. Each member of th population was regarded as nonsyphilitic b cause none presented historical, clinical, la oratory, necropsy, or other acceptable ev dence of syphilitic infection. In order to de conveniently with this large population nonsyphilitics, 2 random samples of 380 pe sons each were drawn from it and labele "control group A" and "control group B The method devised for this random sele tion, and evidence that as regards age, se and color, control groups A and B a actually random samples from the larger no syphilitic population, have been presented chapter 3. Since homogeneity between the groups has been demonstrated, thus verifyi the random sampling method, they have be combined and are treated as one group in th ensuing analysis. A later chapter will demo strate that the mean age at death of both th syphilitic and the nonsyphilitic Negro grou in our series was significantly lower than th comparable mean values for whites. Becau of this observation, the data on Negro pe sons have been excluded from the analys

Breakdowns into sex groups have not been attempted in order not to reduce the size of the statistical samples. The group finally available for analysis consisted of 283 syphilitic and 722 nonsyphilitic white persons.

The frequency of the Warthin lesion in the syphilitic group was compared with its frequency in the control group. All such comparisons were conducted by the method of chi-square. In the statistical procedures significance has been attached to values of $P \leq 0.01$; that is, when the probability of an event occurring by chance was 1 or less than in 100, the result was considered significant.

The review of the histologic preparations was conducted in sequence according to autopsy number and without knowledge as to whether the case under examination belonged to the syphilitic or nonsyphilitic group. This procedure effectively eliminated any unconscious bias that might have been present in the reviewer's mind. Because of Warthin's emphasis on the diagnostic value of the changes in the heart, pancreas, adrenal, liver, and testis, these organs were singled out for examination. The histologic changes sought and their quantitative groupings are given in the appendix under columns 45 to 49 inclusive.

During these microscopic studies repeated reference to Warthin's *New Pathology of Syphilis* was made in order to maintain as constant a standard of diagnosis as possible. Figures 1 to 15 are representative of the tissue changes encountered.

The preparations were fixed in Zenker's solution, rarely in formalin, and embedded in paraffin. The great majority were stained with hematoxylin and eosin, although scattered slides were stained by the methods of van Gieson, Mallory, Heidenhain, and Masson. A small number of Levaditi preparations were present, but no attempt was made to verify the presence or absence of treponemes. The number of slides available was not uniform in each case. In some, only one slide from each organ was on file, in others the sets were incomplete, and in still others, multiple sections of various organs were available, dependent to a large degree on the interest and thoroughness of the individual prosector.

Comparison of Warthin Lesions in the Parenchymatous Organs of Syphilitic and Nonsyphilitic White Persons

General Comments

Early in the survey it became apparent that there was an absence of any qualitative difference between the fibrosis and round cell infiltration observed in the organs of syphilitic persons, and that found in the organs of the nonsyphilitic controls. The distribution of these lesions and their morphologic characteristics were essentially the same in the two groups, which were indistinguishable one from the other on the basis of Warthin's criteria. Moreover, the amount of fibrous replacement and the intensity of the lymphocytic and plasma cell infiltration were extremely variable in both populations, so that the quantitative aspects of these changes could not be utilized in differentiating the syphilitic from the nonsyphilitic groups.

Heart.—When lesions were noted, fibrosis of the interstitium predominated, with varying numbers of plasma cells and lymphocytes. In many instances fibrosis was the outstanding feature but in all such cases, a few scattered round cells could be located on careful search. No effort was made to segregate lesions with predominant fibrosis from those with a cellular infiltration as the outstanding feature. It was observed, however, that the fibroid zones were more prominent beneath the endocardium than in relation to the epicardium. This distribution appeared to occur with equal frequency among the nonsyphilitics and the syphilitics, but the quantitative aspects of this occurrence were not investigated statistically.

Pancreas.—Here also the outstanding change was in the extent of the fibrous tissue deposits, rather than in the numbers of infiltrating inflammatory cells. In rare instances lymphocytes and plasma cells were present in the absence of connective tissue replacement. Occasionally careful search was necessary in order to locate inflammatory cells in cases where fibrosis predominated.

Adrenals.—Small round cell infiltrations were noted in many instances. These occurred most frequently in the medulla.

FIGURE 1.—Heart showing minimum fibrosis and round

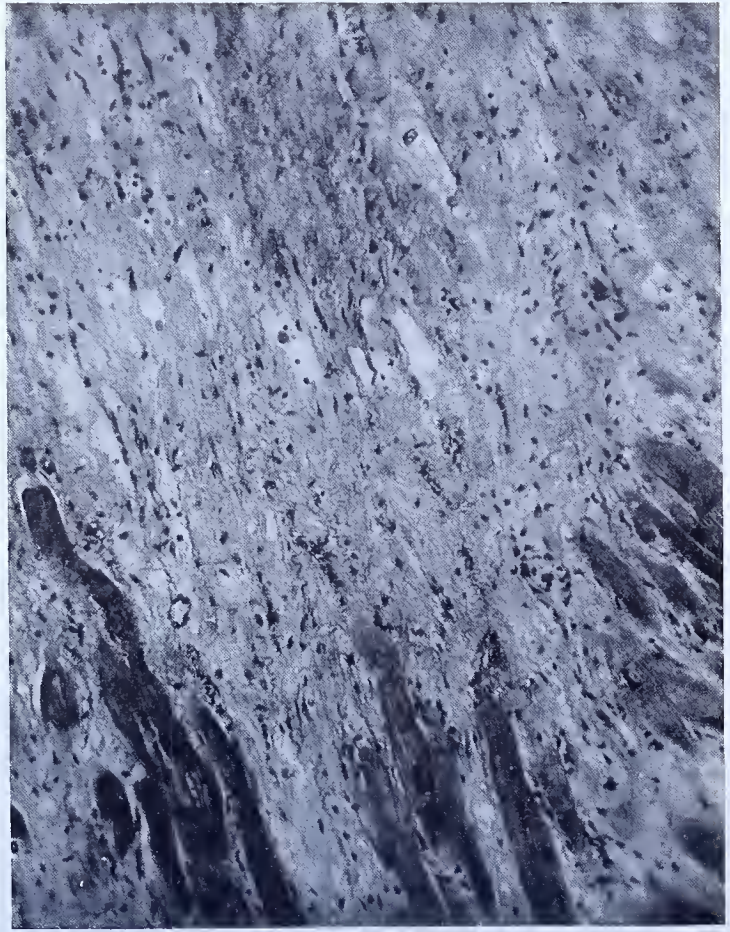

FIGURE 2.—Heart showing maximum fibrosis and round

FIGURE 3.—Heart showing intermediate fibrosis and round cells. Control case. (× 40)

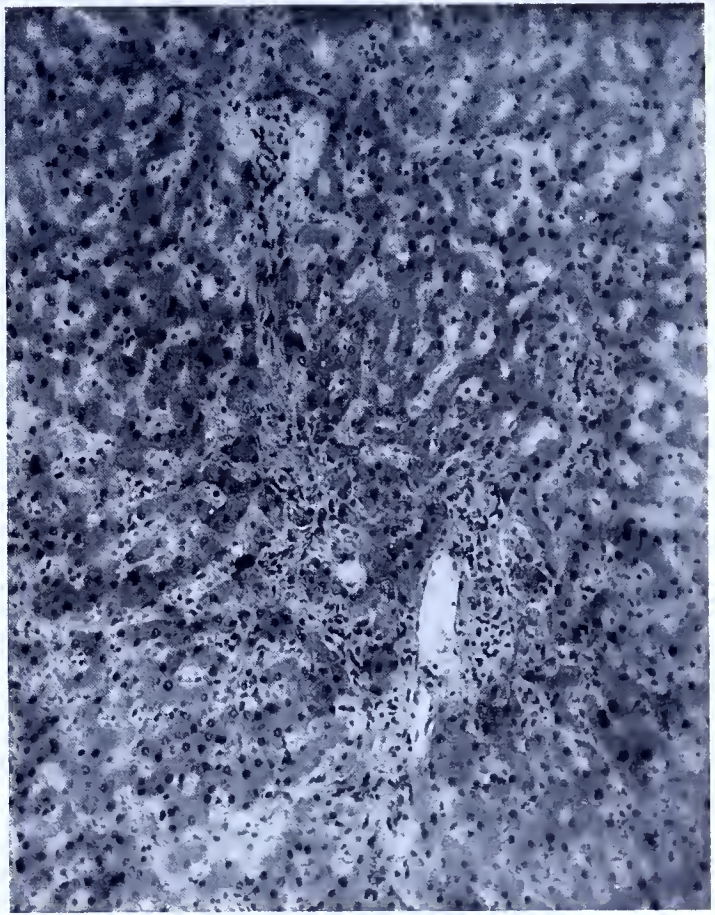

FIGURE 4.—Liver showing minimum fibrosis and round cells. Syphilitic case. (× 175)

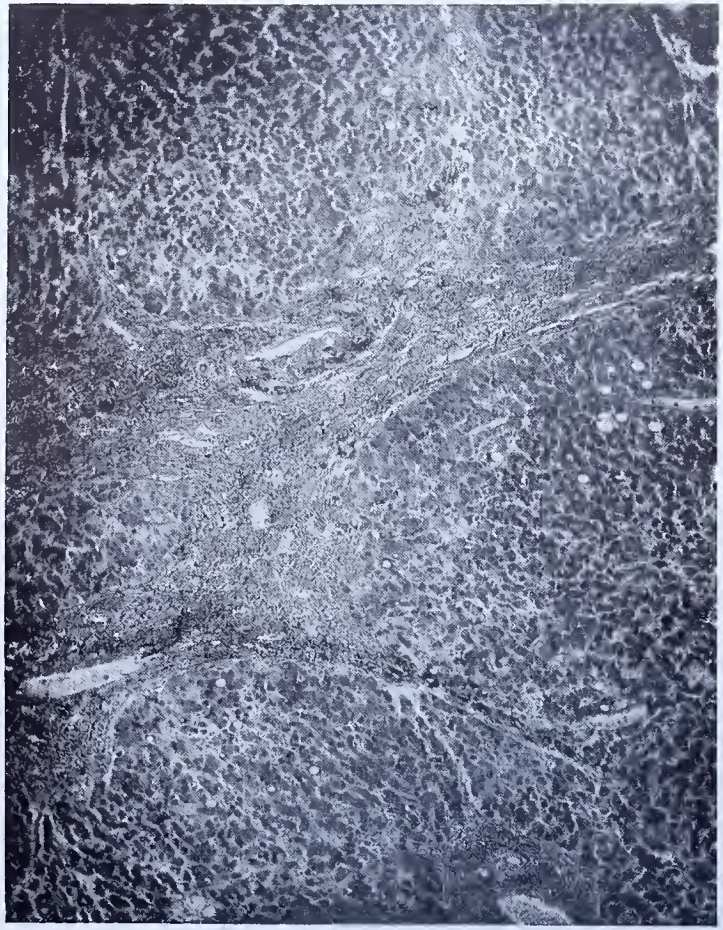

FIGURE 5.—Liver showing maximum fibrosis and round cells. Control case. (× 50)

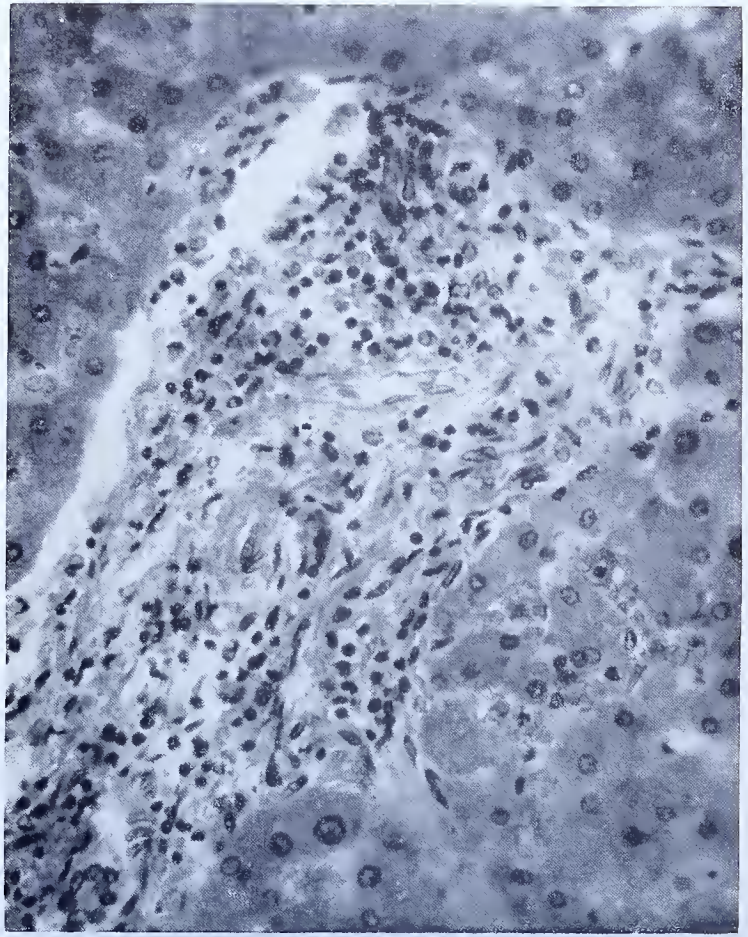

FIGURE 6.—Liver showing round cells. Control case. (× 150)

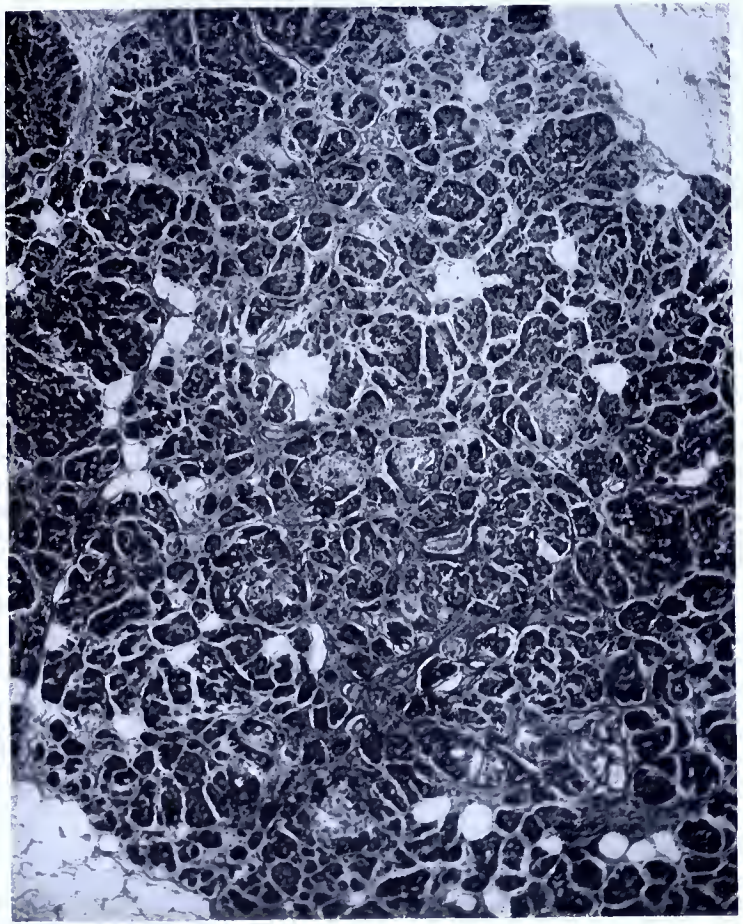

FIGURE 7.—Pancreas showing minimum fibrosis and round cells. Control case. (× 50)

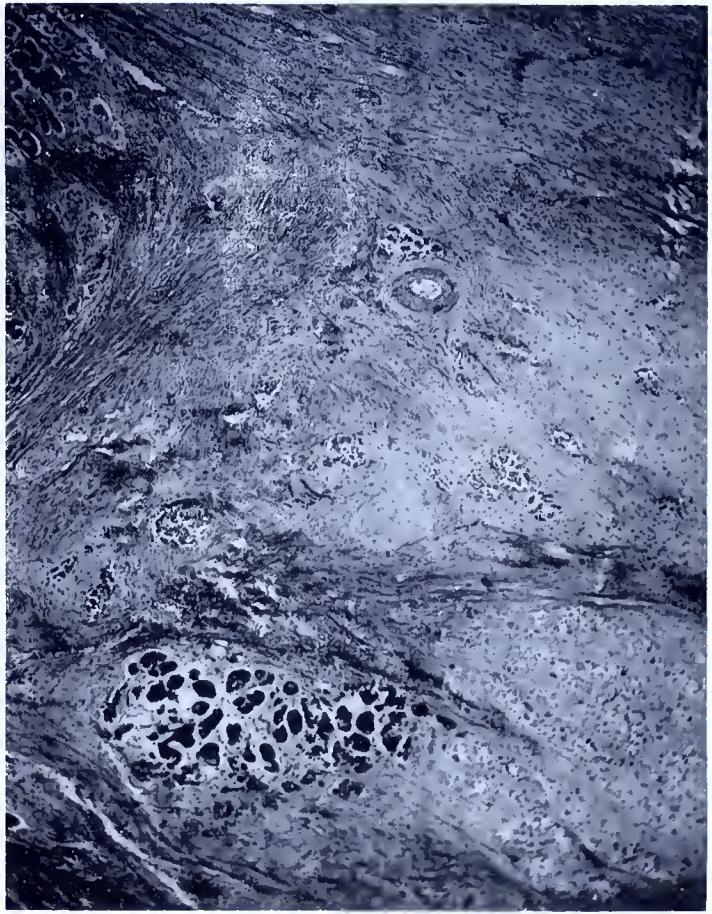

FIGURE 8.—Pancreas showing maximum fibrosis and round cells. Syphilitic case. (× 50)

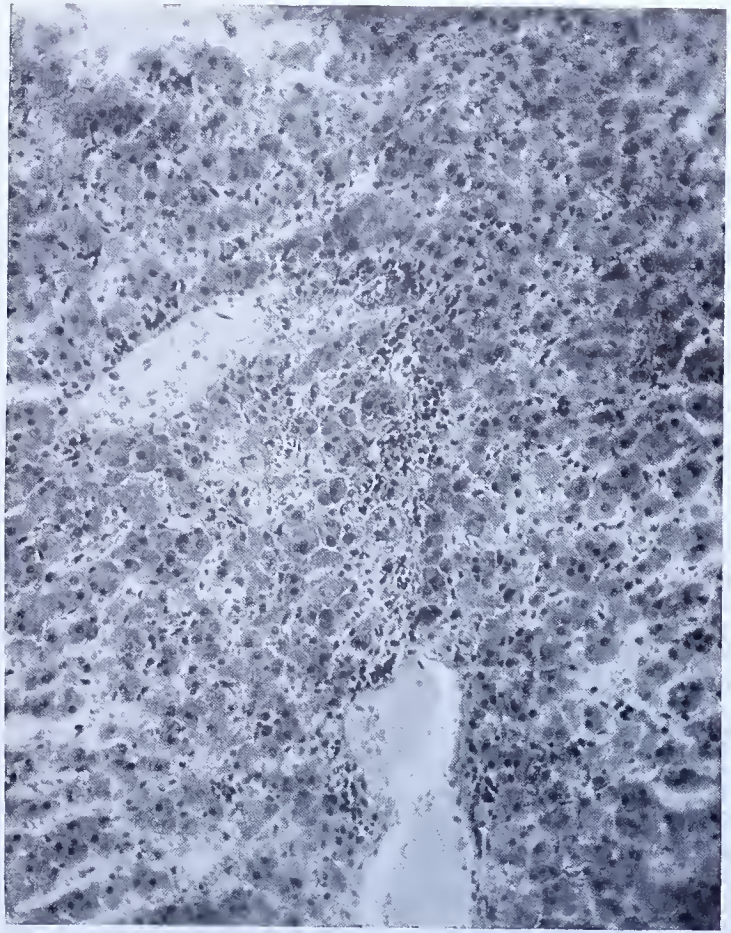

FIGURE 9.—Adrenal showing minimum fibrosis and round cells. Control case. (× 175)

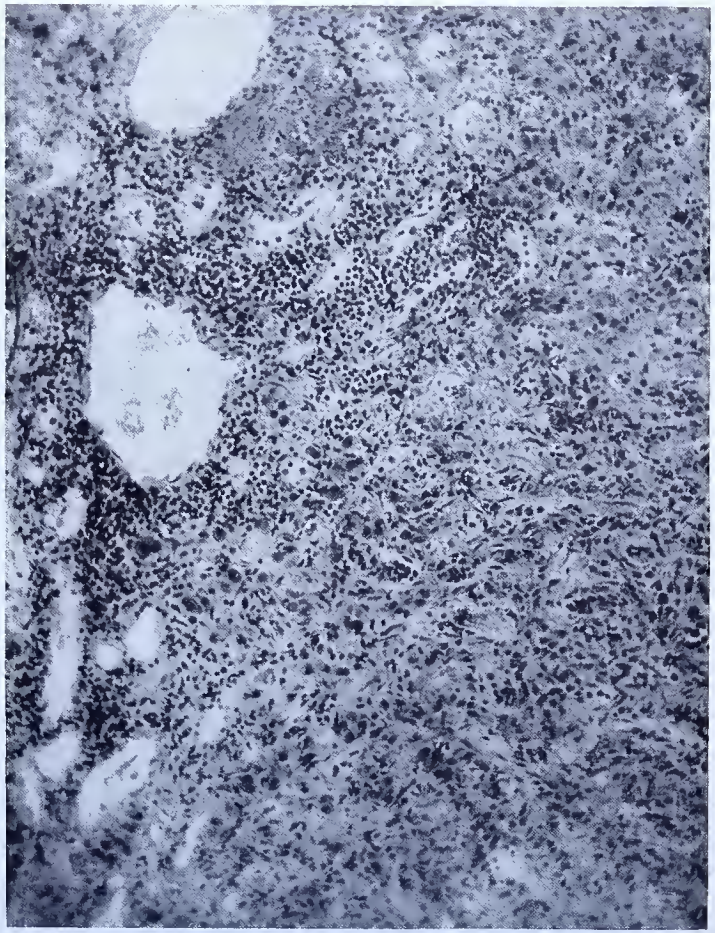

FIGURE 10.—Adrenal showing maximum fibrosis and round cells. Syphilitic case. (× 175)

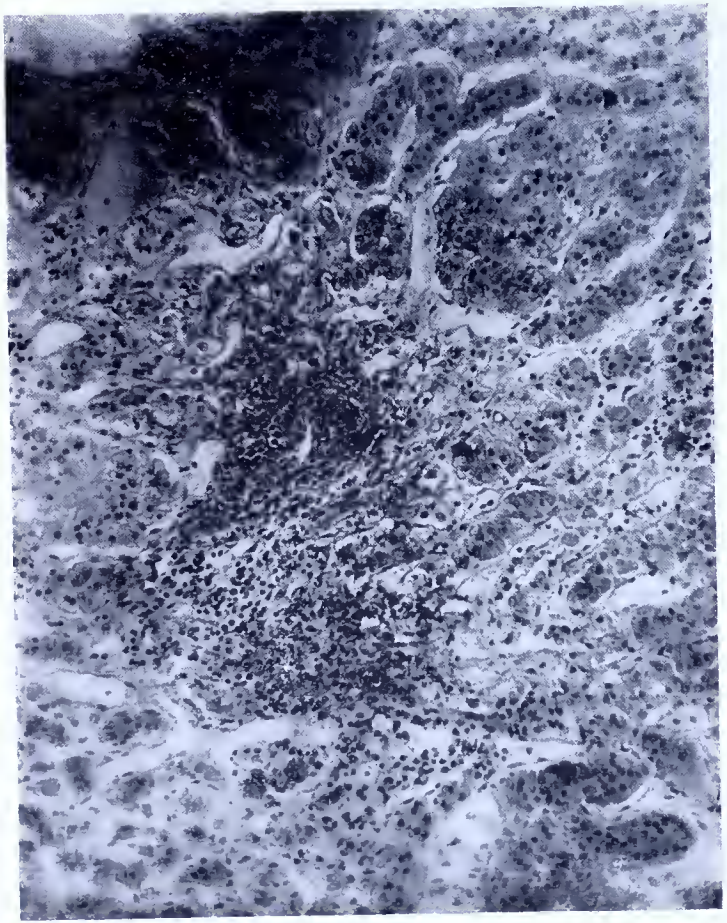

FIGURE 11.—Adrenal showing intermediate round cells. Control case. (× 175)

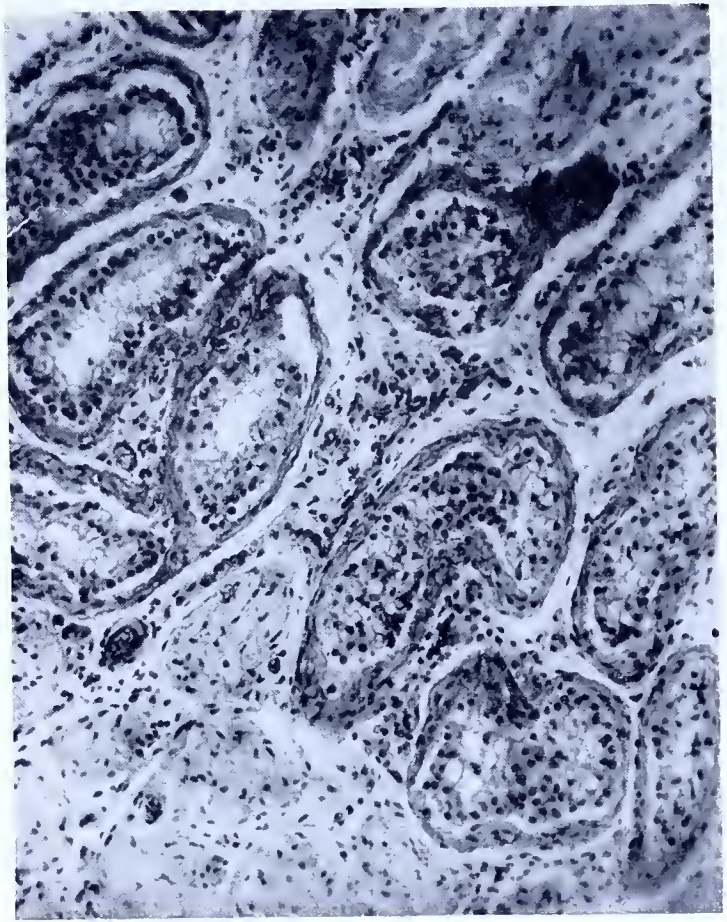

FIGURE 12.—Testis showing minimum fibrosis and round cells. Control case. (× 175)

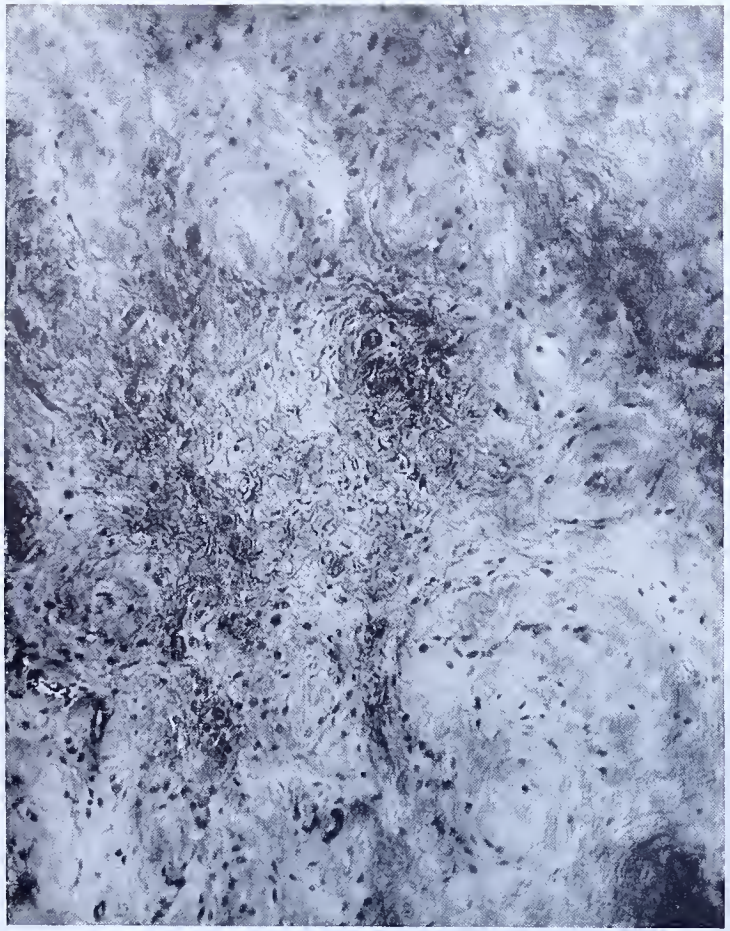

FIGURE 13.—Testis showing maximum fibrosis and round cells. Control case. (× 175)

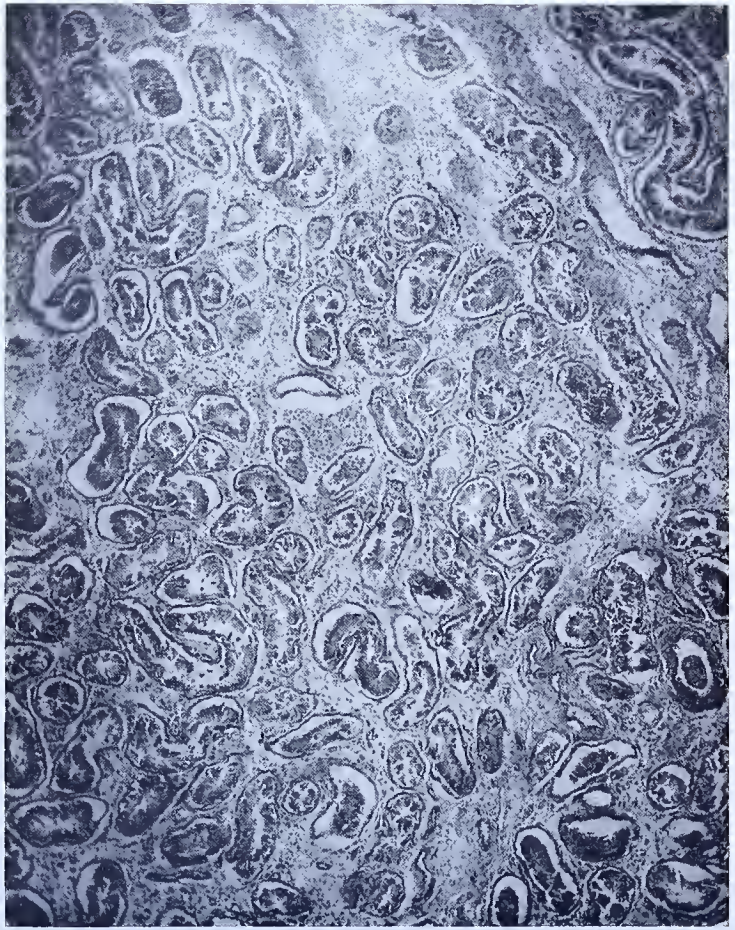

FIGURE 14.—Testis showing maximum atrophy. Syphilitic case. (× 40)

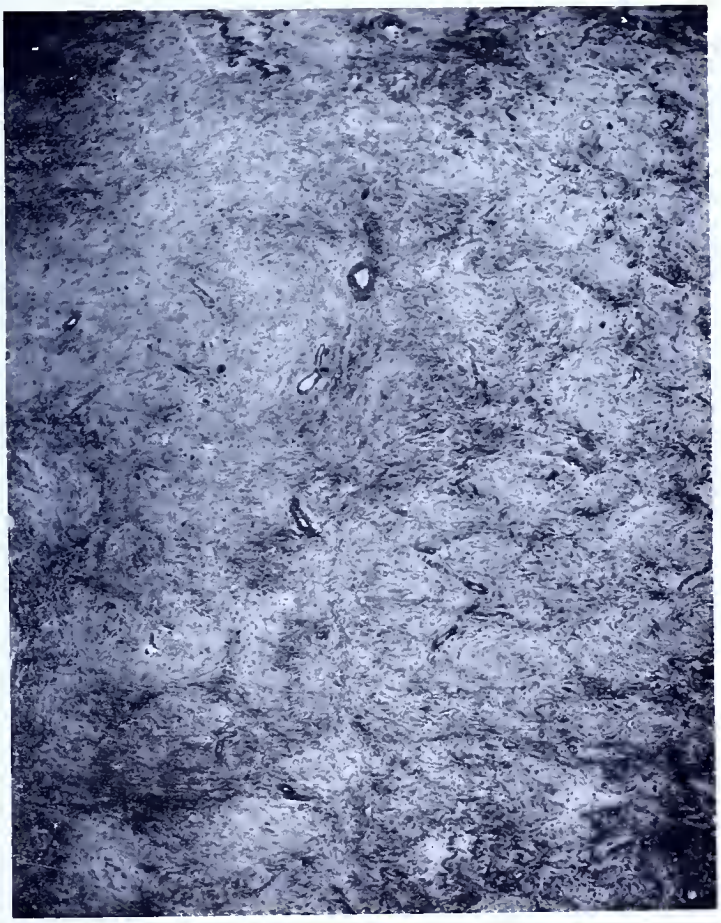

FIGURE 15.—Testis showing maximum fibrosis. Control case. (× 40)

Fibrous tissue deposition was observed so rarely that it did not appear feasible to set up a separate classification based on its presence.

Liver.—Portal fibrosis with lymphocytic and plasma cell infiltration was extremely variable in degree. A group of cases was segregated because of infiltrating inflammatory cells in the portal spaces, in the absence of any increased deposits of connective tissue. These cases were coded under column 46, No. 4, and do not appear in the computations of table 8.

Testis.—Atrophy of the tubules with varying degrees of interstitial fibrosis and cellular infiltrates was the outstanding finding. In many instances the tubular atrophy with basement membrane thickening dominated the picture, but scanty deposits of fibrous tissue and minimal numbers of mononuclear cells were also present.

Incidence

Because of the failure to demonstrate any qualitative differences between Warthin lesions in the organs of syphilitic persons in comparison with nonsyphilitics, other methods of comparison were indicated. These were essentially of a statistical nature. It was concluded that the crucial test of the Warthin hypothesis rested on the demonstration that the lesion which he considered pathognomonic of syphilitic infection occurred more frequently in a population of syphilitic persons than in a population of nonsyphilitics. If such were the case, and if the difference could be shown by statistical methods to be outside the realm of chance occurrence, co siderable weight would be added to Wa thin's conclusions. Final proof would still lacking, however, since even if the Warth lesion were more frequent in a syphilitic th in a nonsyphilitic population, such a findi might be the result of an as yet unknov independent variable other than specific i fection. On the other hand, if the two pop lations did not differ from each other, or the Warthin lesion were found in a great proportion of persons without syphilis th in those known to be infected, the conclusi that the Warthin lesion is nonspecific a due to factors other than syphilitic infecti would seem to be justified. These consider tions have been kept in mind in the co struction of table 8, in which is shown t frequency of Warthin lesions of the hea pancreas, adrenals, liver, and testes in t syphilitic and nonsyphilitic groups.

The proportion of syphilitic persons a of the nonsyphilitic control population wi Warthin changes in the heart was essentia the same, and the two groups were also different as regards Warthin changes in t adrenals, liver, and testes. For all of the organs chi-square was less than 3.841, t lower limit of significance, indicating th any observed difference between the tw populations was well within the limits sampling error.

Warthin lesions were observed in the pa creas of 39.8 percent of the syphilitic grou and in 30.8 percent of the controls. The two values are probably significantly differe (chi-square = 5.61, P = 0.02—), that the observed difference would be expected occur by chance alone about twice in a hu dred such comparisons. The pancreas w

TABLE 8.—*Frequency of Warthin lesions in the parenchymatous organs of syphilitic and nonsyphilitic persons*

Organ	Code for Warthin lesions		Group	Number examined	Lesions found		Chi-squa
	Column	Number			Number	Percent	
Heart	49	2, 3, 4	Syphilitic	239	90	37.7	0.(
			Control	612	233	38.1	
Pancreas	47	2, 3, 4	Syphilitic	211	84	39.8	5.(
			Control	568	175	30.8	
Adrenal	48	2, 3, 4	Syphilitic	186	60	32.3	2.7
			Control	502	130	25.9	
Liver	46	1, 2, 3	Syphilitic	237	70	29.5	0.(
			Control	603	182	30.2	
Testis	45	2, 3, 4	Syphilitic	81	44	54.3	2.3
			Control	151	66	43.7	

NOTE: n=1: Chi-square=6 635, P=0 01; Chi-square=3 841, P=0 05.

thus the only organ of the five studied in which Warthin lesions appeared to occur more frequently among syphilitic persons than among those without specific infection, but the difference here was only probably significant.

In the study of the liver sections a group was segregated because of the presence of round cells in the portal fields without any apparent accompanying fibrosis. This particular tissue change was coded as No. 4, column 46, and does not appear in table 8. It was thought that the frequency of this lesion in the syphilitic and nonsyphilitic populations might throw some light on its etiology and it was therefore investigated. The change was noted in the livers of 109 of the 237 syphilitic persons, and in 295 of the 603 persons comprising the nonsyphilitic group (table 9). The proportion of individuals with this liver lesion in the 2 groups was essentially the same (chi-square = 0.59, N = 1, P = 0.4+) so that specific infection can be excluded as the causative factor.

TABLE 9.—*Frequency of portal round cells without accompanying fibrosis in the livers of syphilitic and nonsyphilitic persons*

	Syphilis present		Syphilis absent		Total
	Observed	Estimated	Observed	Estimated	
Warthin lesions present	109	114	295	290	404
Warthin lesions absent	128	123	308	313	436
Total	237	237	603	603	840

NOTE: n=1, Chi-square=0.59

Of the five organs investigated, the pancreas was the only one in which Warthin lesions occurred significantly more frequently among syphilitics than among nonsyphilitics, and even here the difference was not clearly outside the realm of chance. As indicated in an earlier paragraph, even if this difference were accepted as highly significant, the explanation of the relatively large proportion of nonsyphilitics with the identical lesion is not readily at hand. If syphilitic infection is accepted as one of the agents involved, other factors are certainly operative also. Extending this process of reasoning, the Warthin lesion cannot be accepted as pathognomonic of syphilitic infection by the very fact of its high incidence among uninfected persons. The argument may be presented that the Warthin change is pathognomonic, and by virtue of its presence, the so-called nonsyphilitic persons in our series are actually syphilitic. To this suggestion only one response can be made, that is, the care with which our group of nonsyphilitic persons was selected. None of them had any historical, clinical, or laboratory evidence of the disease, and none of them presented any of the classical changes at autopsy customarily associated with syphilitic infection.

Comparison of Frequency of Warthin Lesions Among Syphilitics With and Without Anatomic Lesions at Autopsy

Comparisons similar to those of the preceding section were made between two groups of syphilitics, one with classical anatomic lesions of syphilis at autopsy, and the other with none of the morphologic changes which in these reports have been accepted as indubitably syphilitic in origin. The criteria for the anatomic diagnosis of syphilis which have been followed in these reports include definite anatomic changes of syphilis of the central nervous system, vascular tree, bone, and parenchymatous organs including liver. Presumptive evidence of syphilis such as orchitis fibrosa, lingua glabia, and so-called syphilitic cirrhosis of the liver was not accepted as indicating morphologic syphilis. Warthin's criteria of lymphocytic and plasma cell infiltration with fibrosis in the parenchymatous organs were likewise not accepted as indicating anatomic evidence of syphilitic infection. The comparisons were conducted by means of the chi-square test of homogeneity, and are shown in table 10. In four of the five organs, any observed difference between the proportions of persons with Warthin lesions in the two groups can be explained by the error of random sampling. Only in the case of the adrenals is there an indication that the difference between the two groups is not due to chance, but even here the difference is not a highly significant one. Thus the presence or absence of definitive syphilitic

TABLE 10.—*Frequency of Warthin changes among syphilitic persons with and without anatomic lesions of syphilis at autopsy*

Organ	Anatomic lesions of syphilis present					Anatomic lesions of syphilis absent					Total	Ch squa
	Warthin lesions present		Warthin lesions absent		Total	Warthin lesions present		Warthin lesions absent		Total		
	Observed value	Expected value	Observed value	Expected value		Observed value	Expected value	Observed value	Expected value			
Heart	47	41.4	63	68.6	110	43	48.6	86	80.4	129	239	2
Pancreas	34	37.8	61	57.2	95	50	46.2	66	69.8	116	211	1
Adrenal	32	25.5	47	53.5	79	28	34.5	79	72.5	107	186	4
Liver	27	31.3	79	74.7	106	43	38.7	88	92.3	131	237	1
Testis	20	22.8	22	19.2	42	24	21.2	15	17.8	39	81	1

lesions was in general not a factor in the production of the tissue alterations described by Warthin.

The Frequency of Warthin Changes in Three Different Autopsy Populations

Between 1909 and 1929, Warthin studied 1,675 persons at autopsy. All were 25 years of age or over. Of this number 494 or 29.5 percent were diagnosed as syphilitic. His findings (*5*) giving the incidence of syphilitic changes by organ in each of the two decades, are shown in table 11. Weller's (*22*) material was obtained from the Haitian General Hospital, Port au Prince, Haiti. The purpose of the study was "to determine (*a*) if the lesions found in this Haitian population in which yaws is so common are like those which in the temperate zone are attributed to syphilis, and (*b*) whether lesions of another type, unknown in a region in which yaws does not exist, would be encountered." W ler's observations, recast to include only p sons over 21 years of age, are also sho in table 11.

Precise statistical comparisons of the th surveys are not necessary to demonstrate t our own findings more closely approxim those of Warthin than do those reported Weller. This is of especial significance in t interpretation of the specificity of the W thin lesion. Weller states: "Because of spec interest in this field, we have established, this laboratory, fairly definite criteria for t diagnosis of syphilis of these organs. Wh these criteria have not received universal ceptance, many have found, as we have, t they are of practical value in determining t presence of visceral syphilis in a gene autopsy population . . . Continued obser tion of the visceral pathology of syphil with constant checking against clinical a serologic data and occasional successes staining spirochetes in regions in which th demonstration is notoriously difficult, has l us to make relatively few changes in the c teria which Warthin proposed." His study

TABLE 11.—*Frequency of Warthin lesions in five organs as reported by three different investigators*

Organ	Warthin						Weller			Yale series	
	1910–1919			1920–1929						Syphilitic	Non syphili
	Cases	Lesions	Percent	Cases	Lesions	Percent	Cases	Lesions	Percent	Percent[1]	Perce
Heart	169	113	66.9	330	216	65.5	142	18	12.7	37.7	38
Pancreas	163	72	44.1	328	98	29.8	[2] 115	[2] 6	5.2	39.8	30
Adrenal	153	47	30.7	320	145	45.3	138	34	24.6	32.3	25
Liver	165	46	27.8	328	102	31.1	139	14	10.1	29.5	30
Testis	137	118	86.1	264	203	76.9	78	42	53.8	54.3	43

[1] See table 8.
[2] Age distribution not given.

NOTE: Warthin's report is based on patients over 25 years of age, Weller's on patients over 21 years of age, and the Yale se on patients aged 20 and over.

the unity or duality of the two diseases, yaws and syphilis, led Weller to conclude that "one of three conditions must exist; either yaws and syphilis are essentially the same disease; or the group of patients here considered has an extremely high incidence of syphilis and the evidences of this disease alone are apparent in the viscera; or yaws and syphilis, if different diseases, produce identical visceral lesions." Weller found no higher, and in fact a lower, incidence of Warthin changes in a Negro population, 70 percent of whom show positive Kahn reactions, than were observed in our population of Caucasians, both syphilitic and nonsyphilitic. Either the Warthin lesion actually occurs less frequently among Negroes of Haiti, where yaws is very common, than it does among whites with and without syphilis, or the lesion represents a nonspecific change. The first of these alternatives appears unlikely in view of Weller's comments on the identity of yaws and syphilis.

The Warthin Lesion and the Aging Process

If the Warthin lesion is not pathognomonic of syphilitic infection, what factor or factors are responsible for its presence? Many possible causative determinants can be postulated, among which are nonspecific concomitant or antecedent infections, disorders produced by hormone imbalance or nutritional and more particularly vitamin deficiencies, and changes associated with increasing age. Each of these possibilities, as well as others not readily apparent, offers a fruitful subject for investigation, but the last is the only one which can be elucidated by our own material. Is there any relation between longevity and the incidence of Warthin lesions? Is tissue fibrosis with cellular infiltrates related to diminished local nutrition resulting from the vascular sclerosis accompanying increasing age? The phrase "aging process" is employed herein with the full knowledge that what we are dealing with may not be the aging process per se, but the fact that with increasing age there is increasing opportunity for exposure to factors both exogenous and endogenous which produce structural tissue changes.

In tables 12 and 13 are shown the incidence of Warthin lesions in the syphilis and control groups according to organ and decennia. The summated incidence of these lesions in persons under and over 60 years of age is also given in these tables, and depicted graphically in chart 5. From the tables it is seen that the proportion of cases in which Warthin lesions were found increases steadily in most tissues and in both groups, with increasing age. In the syphilis group the proportion of cases with Warthin changes in the heart, adrenal, liver, and testis was significantly greater in the "60 and over" class than in the "under 60" class. (Chi-square: heart = 8.46, adrenal = 12.33, liver = 6.85, testis = 10.80). Warthin lesions of the pancreas were found in a greater proportion of syphilitics in the "60 and over" group than in the

TABLE 12.—*Number of syphilitic cases examined and number and percent in which Warthin lesions were found, by age and tissue*

Age	Heart			Pancreas			Adrenal			Liver			Testis		
	Cases	Warthin lesions found		Cases	Warthin lesions found		Cases	Warthin lesions found		Cases	Warthin lesions found		Cases	Warthin lesions found	
		Number	Percent		Number	Percent		Number	Percent		Number	Percent		Number	Percent
20–29	8	0	..	6	0	..	6	0	..	5	0	..	3	0	
30–39	33	8	24.2	31	14	45.2	30	5	16.7	39	12	30.8	8	1	12 5
40–49	57	18	31.6	45	16	35.6	43	8	18.6	55	14	25.5	19	7	36 8
50–59	62	24	38.7	57	21	36.8	41	15	36.6	59	12	20.3	20	12	60.0
Total under 60	160	50	31.3	139	51	36.7	120	28	23.3	158	38	24.1	50	20	40.0
60–69	55	27	49.1	53	24	45.3	50	24	48.0	56	24	42.9	22	17	77.3
70 and over	24	13	54.2	19	9	47.4	16	8	50.0	23	8	34.8	9	7	77.8
Total 60 and over	79	40	50.6	72	33	45.8	66	32	48.5	79	32	40.5	31	24	77.4
All ages	239	90	37.7	211	84	39.8	186	60	32.3	237	70	29.5	81	44	54.3

TABLE 13.—*Number of nonsyphilitic cases examined and number and percent in which Warthin lesions were found, by age and tissue*

Age	Heart			Pancreas			Adrenal			Liver			Testis		
	Cases	Warthin lesions found		Cases	Warthin lesions found		Cases	Warthin lesions found		Cases	Warthin lesions found		Cases	Warthin lesions found	
		Number	Percent		Number	Percent		Number	Percent		Number	Percent		Number	Pe ce
20–29	66	12	18.2	57	4	7.0	56	5	8.9	61	25	41.0	16	7	43
30–39	79	15	19.0	80	17	21.2	77	11	14.3	79	23	29.1	21	5	23
40–49	99	34	34.3	93	26	28.0	89	25	28.1	97	28	28.9	28	12	42
50–59	148	59	39.9	127	50	39.4	105	30	28.6	141	44	31.2	32	10	31
Total under 60	392	120	30.6	357	97	27.2	327	71	21.7	378	120	31.7	97	34	35
60–69	109	57	52.3	105	41	39.0	82	24	29.3	109	25	22.9	28	12	42
70 and over	111	56	50.5	106	37	34.9	93	35	37.6	116	37	31.9	26	20	76
Total 60 and over	220	113	51.4	211	78	37.0	175	59	33.7	225	62	27.6	54	32	59
All ages	612	233	38.1	568	175	30.8	502	130	25.9	603	182	30.2	151	66	43

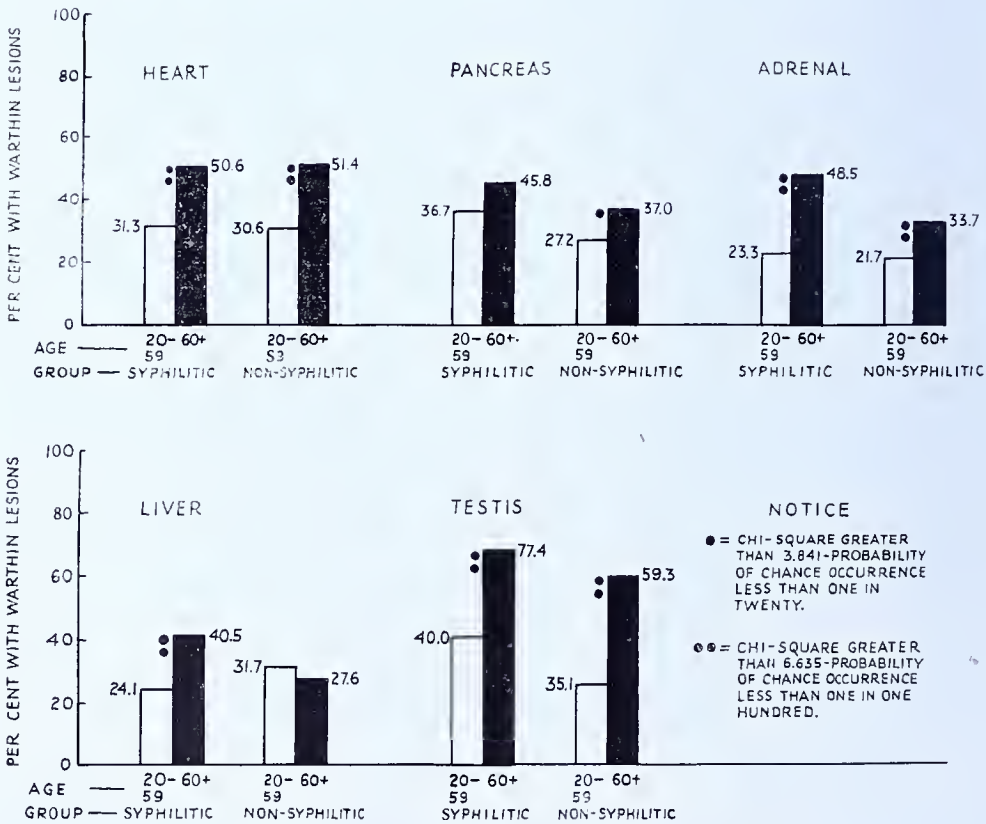

CHART 5.—Incidence of Warthin lesions in syphilitic and nonsyphilitic groups according to age, class, and tissue.

"under 60" class, but the difference was not significant (chi-square = 1.65).

The nonsyphilitic group gave essentially the same results. Here the proportion of persons with Warthin changes in the heart, adrenal, and testis was significally greater in the "60 and over" class than in the "under 60" class (chi-square: heart = 25.74, adren = 8.56, testis = 8.26). In the pancreas t difference between the two age classes w in the same direction but only probab significant (chi-square = 4.21). The liver the nonsyphilitic group was the only orga of those studied which showed a slight

higher proportion of cases with Warthin lesions in those under 60 than in those over 60, but the difference here was insignificant (chi-square = 1.18).

Cross comparisons between the syphilitic and nonsyphilitic groups in each age class were also made. In the "under 60" class only the pancreas showed a suggestive difference between the proportions of syphilitics and nonsyphilitics with Warthin lesions, the chi-square values for the other 4 organs indicating an absence of significant heterogeneity (chi-square: pancreas = 4.33, heart = 0.02, adrenal = 0.13, liver = 3.17, testis = 0.35). In the "60 and over" age category, the adrenals and liver showed a borderline significant difference in the proportions of syphilitics and nonsyphilitics with Warthin changes, but the two groups were homogeneous as regards Warthin changes in the other three organs (chi-square: adrenal = 4.45, liver = 4.59, heart = 0.01, pancreas = 1.77, testis = 2.89). In not a single one of the 10 comparisons was the value for chi-square greater than 6.635, at which level the probability of chance as a factor accounting for any observed difference is less than 1 in a hundred.

These findings indicate that so far as the syphilis population is concerned, age is related to the incidence of Warthin lesions, more persons with Warthin lesions falling into the older age categories than persons without these changes. With the exception of the liver, the observations on the nonsyphilitic population parallel those on the syphilitic population. This is not to be interpreted as indicating that age is the only factor concerned in the production of the Warthin phenomenon, but it is clearly one variable which must be considered when an explanation for these lesions is sought.

Weller's data on the adrenal, liver, and testis tend to confirm the relation between age and the presence of the Warthin tissue changes. Twenty of eighty-nine persons between 21 and 60 years of age, or 22.5 percent, had these changes in the adrenals, as compared with 14 of 49 persons, or 28.6 percent, of those over 60 years. For the liver, 5 of 89 persons between 21 and 60 years, or 5.6 percent, showed the histologic changes, as compared with 9 of 50 persons in the older age group (18.0 percent). Lesions of the testis showed a similar differential between the older and younger age groups. There were 26 out of 55 persons under 60 years, or 47.3 percent, and 16 out of 23 persons over 60, or 69.6 percent, with these lesions in the testis. The heart findings, however, were different, for here fewer persons with Warthin changes were over 60 than under 60 years of age.

The significance of the aging process in relation to the Warthin lesion of fibrosis and round cell infiltration, in both syphilitic and nonsyphilitic populations, has been demonstrated. Other factors may also be operative, but regardless of what they may be, the evidence does not support Warthin's contention that the microscopic lesion which he described so carefully is pathognomonic of syphilitic infection.

MORTALITY AND MORBIDITY FINDINGS IN THE YALE AUTOPSY SERIES [1]

This chapter will discuss the incidence of the anatomic changes produced by syphilitic infection among individuals aged 20 and over who were observed at necropsy in the Department of Pathology at the Yale University School of Medicine during the period 1917 to 1941. Three groups, controlled by appropriate observations on the nonsyphilitic population, will be considered. These are: (1) those with morphologically demonstrable tissue changes of syphilis, who, in the opinion of the prosector, supported by the judgment of the reviewers, died primarily as a result of these lesions; (2) those with anatomic changes ascribed to syphilitic infection who died primarily from some other disease process; and (3) those with historical or clinical or laboratory evidence of syphilitic infection during life in whom anatomic changes attributable to syphilis could not be demonstrated at autopsy.

In the first chapter it was concluded that the great variability in the incidence of syphilitic changes at autopsy reported by different investigators was largely the result of varying criteria for the morphologic diagnosis of syphilis. A brief statement concerning our own criteria is in order at this time. These autopsies were conducted by many different prosectors associated with the Department during a period of over 20 years. All diagnoses were based upon gross and microscopic examinations and all were checked and confirmed by group discussion among members of the Department at the time of the necropsy. The criteria generally observed were those enunciated by Nickel (*21*), that is, definite anatomic changes of syphilis of the central nervous system, vascular tree, bone and parenchymatous organs including liver. Presumptive evidence of syphilis such as oo chitis fibrosa, lingua glabia, and so-called syphilitic cirrhosis of the liver were not accepted as indicative of morphologic syphilis. Warthin's criteria of lymphocytic and round cell infiltration with fibrosis in liver, heart, adrenals, testes, and pancreas were not followed.

Syphilis Morbidity

A total of 3,907 individuals over 20 years of age was autopsied. Of these, 90 had anatomic lesions of syphilis which were primarily responsible for death, 66 showed anatomic lesions of syphilis but died primarily as the result of some other disease process, and 224 individuals with historical or laboratory or clinical evidence of syphilis had no demonstrable syphilitic lesions at autopsy. The distribution of these 3 groups by sex is shown in table 14. The total, 380, represents 9.7 percent of 3,907 adult autopsies in this series. This, as a matter of fact, is the minimum rather than the maximum incidence of syphilis in the autopsy population, since a certain number of those comprising this population were undoubtedly not included in the syphilitic group because of inadequate or incomplete clinical data. This is especially true of many who died shortly after admission and also of a large number of medical examiner's and coroner's cases brought to the hospital for autopsy.

The 9.7 percent incidence of syphilis in our autopsy group is of especial significance in view of Parran's oft-quoted statement "Syphilis strikes 1 out of every 10 adults." This conclusion is based upon the exhaustive statistical analysis conducted by Vonderleh

[1]This chapter is a revision of the article *Studies in Syphilis. III. Mortality and Morbidity Findings in the Yale Autopsy Series,* by Paul D. Rosahn and Bernard Black-Schaffer, which appeared in the *Yale Journal of Biology and Medicine,* vol. 15, p. 587, 1943.

TABLE 14.—*Presence or absence of anatomic lesions of syphilis at autopsy in Yale series according to sex*

Group	Male		Female		Total	
	Number	Percent	Number	Percent	Number	Percent
Anatomic lesions causing death	68	25.7	22	19.0	90	23.7
Anatomic lesions not related to cause of death	50	19.0	16	13.8	66	17.4
Total anatomic lesions	118	44.7	38	32.8	156	41.1
No anatomic lesions	146	55.3	78	67.2	224	58.9
Total	264	100.0	116	100.0	380	100.0

and Usilton (*25*), who computed the annual attack rate per 100,000 individuals born alive and followed throughout life. In spite of a comparatively low annual attack rate, they showed that when cumulated so as to indicate the probability of acquiring syphilis by any given age, 10,000 people out of every 100,000 born alive will have acquired syphilis before the age of 50 years has been reached. This method of analysis begins at birth and projects the probability of acquiring syphilis into any given age period in the future. Our own study reverses the process. We have looked back from the vantage point of life's end, that is, from the time of death, and have retrospectively studied the clinical histories of a large autopsy population. Roughly 10 percent of our autopsy population presented clinical or other evidence of syphilis. This finding is identical with the conclusion reached by Vonderlehr and Usilton, and serves as corroborative evidence, reached by a totally different approach, that syphilis attacks 1 out of 10 adults.

Frequency of Anatomic Lesions at Autopsy

From table 14 it is apparent that 156, or 41.1 percent of the 380 syphilitic individuals coming to autopsy had morphologic changes recognized as syphilitic. Melchior (*19*) and Frates (*18*) are the only other authors from whose material corresponding categories could be obtained, and of the two there is internal evidence that Melchior's clinical observations were the more careful. Out of 353 autopsied syphilitics, Melchior found tissue changes of syphilis in 245, or 69.4 percent, while the corresponding finding by Frates is 418, or 82.9 percent, of 504 syphilitics. Summating these findings without regard to variety or intensity of treatment or to criteria for the anatomic diagnosis of syphilis, approximately from one-half to two-thirds of syphilitics show morphologic tissue changes of syphilis at autopsy.

The group of syphilitics with no specific anatomic lesions at autopsy challenges explanation. Was the clinical diagnosis in error? If not, did spontaneous or therapeutic cure, both biologic and morphologic, take place? Did tissue lesions, originally present, completely regress, leaving no residual changes to draw attention to earlier alterations in morphology? Or were tissue changes of a specific nature actually present at autopsy and unrecognized as such?

Each of these questions requires further study, but an interesting side light on them is shown in table 15. The treatment status of 194 of the 224 syphilitics with no lesions at autopsy was known. Of this group, 109, or 56 percent, had received no treatment of any kind. More than half of this untreated group, 63, or 58 percent, were diagnosed as latent syphilitics on their last admission, that is, the only evidence of the disease was serologic positivity. It is apparent then that about half of the syphilitics with no demonstrable lesions at autopsy had never received treatment, and furthermore that a majority of these were diagnosed as syphilitic on the basis of accepted serologic criteria. It should be stated that the necropsy included an examination of the brain in 129 of these 224 individuals. In this group, therefore, tissue changes either did occur and were unrecog-

TABLE 15.—*Clinical status on last admission and history of treatment of 224 syphilitics with no anatomic lesions of syphilis at autopsy*

Status on last admission	Received treatment	Never treated	Treatment not known	Total
Cured	24	10	5	39
Latent syphilis	27	63	11	101
Organic changes clinically diagnosed	23	14	2	39
Syphilis not diagnosed [1]	11	22	12	45
Total	85	109	30	224

[1] This group had a past history of syphilis which was not noted or was overlooked on the last admission.

nized, or regression of lesions took place with or without treatment, or lesions never developed.

Syphilis as a Primary Cause of Death

Ninety out of the one hundred and fifty-six individuals with anatomic lesions at autopsy died primarily as a result of their syphilis (table 14). This is 57.6 percent of the group, or 23.7 percent of the 380 syphilitics and 2.3 percent of the total population of 3,907 individuals (chart 6). Table 16 summarizes the findings of other reporters. Of 2,003 syphilitics with tissue changes, 1,463, or 73 percent, died primarily as the result of the specific infection. This represents 3.6 percent of the total of 39,907 autopsies.

What were the chances of a fatal outcome once a clinical diagnosis of syphilis was made? In our group of 380 syphilitics, there were 320 with historical or clinical or serologic evidence of syphilis. Of this group, 96 had post-mortem changes compatible with a diagnosis of syphilis, and 57 died primarily from their syphilis. Summarizing this experience, once a diagnosis on clinical or labora tory evidence was made, 3 out of 10 syphi itics developed significant tissue lesions, and out of 5 died therefrom. The converse even more striking, for in 7 out of 10 case tissue changes did not occur, and in 4 out 5 syphilis did not cause death. These result do not take into consideration the condition ing influence of treatment, its intensity, time of initiation.

TABLE 16.—*Syphilis as a primary cause death in individuals over 20 years of ag according to six reporters*

Author [1]	Column No. 1	2	3		
	Total autopsy population	Number with anatomic syphilis	Deaths due primarily to syphilis		
			Number	Percent of column 2	Percen of column
Manohar (*8*)...	2,721	444	323	72.7	11.
Koppisch (*9*)...	665	76	39	51.3	5.
Guldberg (*23*)..	8,235	481	349	72.5	4.
Melchior (*19*)..	4,594	245	140	57.1	2.
Bell (*10*).....	19,785	601	522	86.9	2.
Yale series.....	3,907	156	90	57.6	2.
Total....	39,907	2,003	1,463	73.0	3.

[1] Figures in parentheses are bibliographic references.

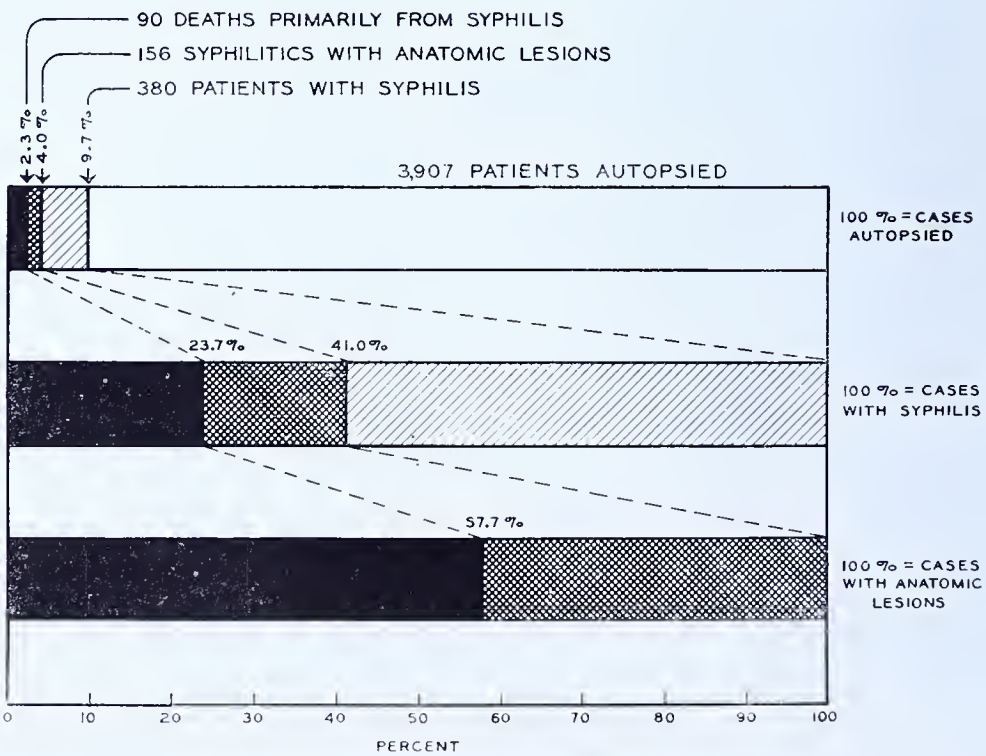

CHART 6.—Proportion of syphilitics, syphilitics with anatomic lesions, and deaths from syphilis in Yale series.

Incidence and Age Distribution of Syphilis in the Negro

Many specialized studies of the pathology of syphilis and a large number of clinical and serologic investigations have been published, but only two papers have been found which give the racial distribution of individuals with anatomic lesions at autopsy. Of necessity, European pathologists have confined their remarks almost exclusively to findings on Caucasians. Ogden (*12*), in New Orleans, found an incidence of 3.9 ± 0.4 percent among whites and 10.5 ± 0.5 percent among Negroes, while Koppisch (*9*) found 8.6 ± 1.4 percent of his whites and 14.9 ± 2.3 percent of his Negro population with syphilitic lesions at autopsy (table 17). The comparable figures for our own study are 3.3 ± 0.3 percent and 13.8 ± 2.2 percent. Table 17 also indicates the distribution by race of the total autopsy populations studied. Ogden's series included 57.8 percent Negroes, while Koppisch had 38.4 percent Negroes in his series, and our own study was based upon a population comprising 6.3 percent Negroes. In spite of these relatively wide fluctuations in the Negro components of the three series, it is noteworthy that the incidence of syphilis among Negroes in the three studies is essentially the same with an average of 13.1 percent. Giving due weight, however, to the numbers involved in each series, there were 400 Negroes with anatomic lesions of syphilis, or 11.0 percent of a total Negro autopsy population of 3,622.

In contrast to the relatively similar incidence of syphilis found in Negroes in New Orleans, Puerto Rico, and New Haven, there is dissimilarity in the incidence among whites. In this instance the New Haven and New Orleans findings do not differ from each other, but the frequency of anatomic lesions in whites in both of these localities is significantly lower than in Puerto Rico.

Of 97 Negroes in our syphilitic group of 380, 34 individuals, or 35 percent, had anatomic lesions of syphilis (table 18). The comparable figure for the white population of 282 syphilitics was 122, or 43.3 percent. The difference between these two findings is statistically not significant, and it may be concluded therefore that in our series there was no greater frequency of anatomic lesions among syphilitic Negroes than among syphilitic whites. However, in spite of this finding, more whites with anatomic lesions (73 out of 122 cases, or 60 percent) died primarily as the result of their syphilis than did Negroes (17 out of 34 cases, or 50 percent). This is shown in table 18. Although the difference between these values is not statistically significant, the findings are contrary to the generally accepted belief that syphilis runs a more fatal course among Negroes than among whites.

The 97 syphilitic Negroes had a mean age at death of 47.0 ± 1.44 years, in contrast

TABLE 17.—*Syphilitics with anatomic lesions in white and Negro autopsy populations*

Author	White			Negro		
	Total population	Syphilitic		Total population	Syphilitic	
		Number	Percent		Number	Percent
Ogden	2,280	89	3.9±0.4	3,128	329	10.5±0.5
Koppisch	397	34	8.6±1.4	248	37	14.9±2.3
Yale series	3,661	122	3.3±0.3	246	34	13.8±2.2
Total	6,338	245	3.9±0.2	3,622	400	11.0±0.5

TABLE 18.—*Presence or absence of anatomic lesions of syphilis at autopsy in Yale series according to race*

Group	White		Negro		Total	
	No.	Percent	No.	Percent	No.	Percent
Anatomic lesions causing death	73	25.9	17	17.5	90	23.8
Anatomic lesions not related to cause of death	49	17.4	17	17.5	66	17.4
Total anatomic lesions	122	43.3	34	35.0	156	41.2
No anatomic lesions	160	56.7	63	65.0	223	58.8
Total	282	100.0	97	100.0	379	100.0

NOTE: 1 Oriental omitted

to 52.65 ± 0.81 years, the mean age at death of the 282 white syphilitics. These two values are significantly different, indicating that on the average the syphilitic Negro died at a younger age than the syphilitic white. This is in agreement with the general conclusions of Usilton and Miner (*26*), who plotted death curves for white and Negro males with acquired syphilis, utilizing the material of the Cooperative Clinical Group. The same significant differential in mean age was observed when contrasting the nonsyphilitic white populations of control groups A and B with the nonsyphilitic Negro population in the total series of 3,907 cases (chart 7). Moreover, there was no noteworthy difference between the mean age at death of the syphilitics of either race and the mean age of the comparable nonsyphilitic racial groups. From this it appears that in our experience syphilis had no greater influence on Negroes than on whites so far as the mean age at death was concerned, although Negroes, with or wi out syphilis, died younger than whites.

It has been shown (*27*) that, according the 1929-31 figures, the life expectancy birth for Negro males and females is 47. years and 49.53 years, respectively, compar to 59.31 and 62.83 years for white males a females. The shorter life expectancy of t Negro has been attributed largely to syp ilis. In our own experience cited above, th was no difference between the mean age death of nonsyphilitics as contrasted wi syphilitics, and this was true for Negroes well as for whites. These figures suggest th the shorter life expectancy of Negroes, bo syphilitic and nonsyphilitic, as contrasted whites, may be due not to the effects syphilis per se, as has been suggested, b rather to nonspecific factors such as soci and economic influences which adversely i fluence the life expectancy of Negroes general.

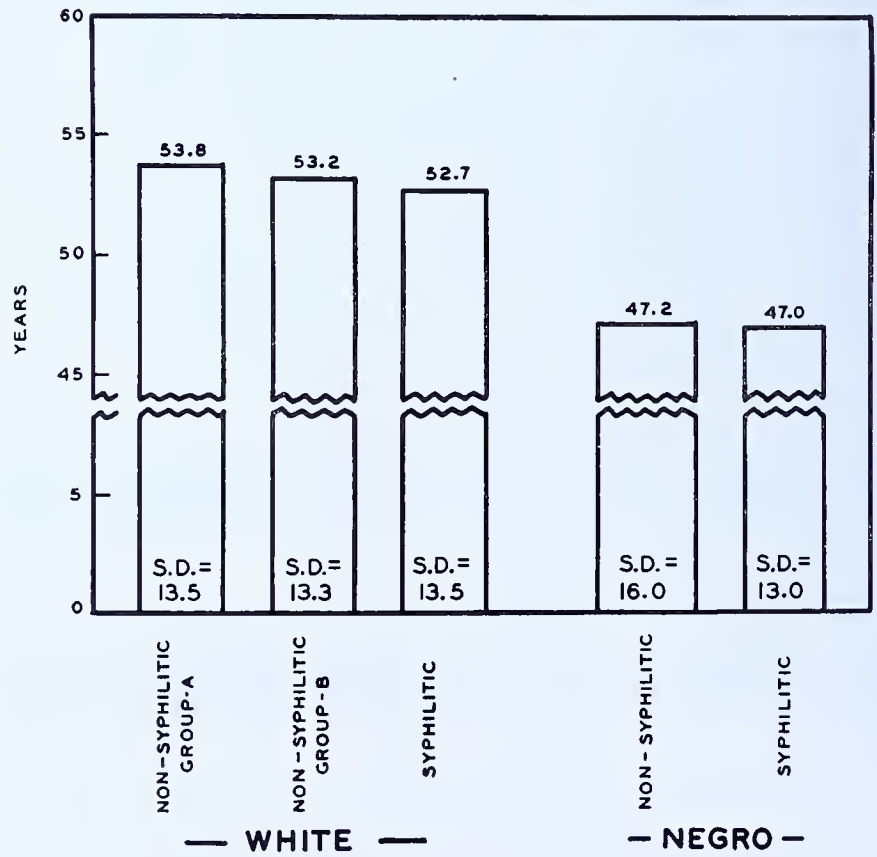

CHART 7.—Mean age and standard deviation of white and Negro syphilitics and nonsyphilitics.

Syphilis and Sex

The 3,907 individuals in our total population were grouped into 2,496 males (63.8 percent) and 1,411 females (36.2 percent). From table 14 it is seen that the 156 syphilitics with anatomic lesions at autopsy consisted of 118 males (75.6 percent) and 38 females (24.4 percent). There were thus significantly more males among the syphilitics with anatomic lesions than there were in our total population (chi-square = 9.38, n = 1, P = < 0.01). In terms of incidence, syphilitic males with lesions constituted 4.7 percent of the male population and syphilitic females with lesions composed 2.7 percent of the female population. These findings are in general similar to those previously reported in a review of the literature and substantiate the general impression that syphilitic lesions at autopsy are twice as frequent in the male as in the female. This might, of course, be explained by a lower rate of exposure or of susceptibility for females than for males. However, when our total group of syphilitics is considered, those with and those without anatomic lesions (table 14), 38 of 116 female syphilitics (32.8 ± 4.4 percent) had anatomic lesions of syphilis at autopsy, as compared with 118 out of 264 males (44.0 ± 3.1 percent). These two rates are probably significantly different (t = 2.1, P = < 0.05), and indicate that anatomic lesions developed less frequently in the female syphilitic than in the male. Thus, even in a group of women diagnosed as syphilitics on clinical or historical or other evidence, syphilitic lesions occurred less frequently than in a comparable group of men. The conclusion seems justified that sex is an important factor in resistance to the tissue changes of syphilis.

This generalization is independent of race, as is shown in table 19. Whites and Negroes in control group A both had an identical sex distribution, that is, 60 percent males and 40 percent females. Similarly white and Negro syphilitics with anatomic lesions also had an identical sex distribution, 75 percent males and 25 percent females. Thus the sex distribution among our syphilitics with lesions at autopsy was essentially identical regardless of race.

TABLE 19.—*Sex distribution by race in control group A and among syphilitics with anatomic lesions of syphilis at autopsy*

Group	Sex	White		Colored		Total
		No	Percent	No	Percent	
Control Group A	Male	216	59.5	10	58.9	226
	Female	147	40.5	7	41.1	154
Total		363	100.0	17	100.0	380
Syphilitics with lesions at autopsy	Male	93	76.3	25	73.6	118
	Female	29	23.7	9	26.4	38
Total		122	100.0	34	100.0	156

Syphilis and Longevity

Since it has been shown in a previous section that Negroes, both syphilitic and nonsyphilitic, die at a significantly earlier mean age than whites, the following analysis deals solely with white individuals. Males and females have been grouped together in order to increase the number of observations.

Table 20 shows the mean age at death of the whites in control groups A and B, and in the syphilis group. The latter has been further broken down into its constituent categories. There is no significant difference between any of the values shown in the table. In our material, therefore, there was no indication that syphilis had any effect on the mean age at death regardless of whether or not it resulted in specific tissue changes, and whether or not it was primarily responsible for death.

TABLE 20.—*Mean age at death of nonsyphilitic and syphilitic white individuals in Yale autopsy population*

Group	Number	Mean age in years
Nonsyphilitic:		
Control A	355	53.9±0.71
Control B	353	53.2±0.71
Syphilitic:		
Without lesions	157	51.5±1.12
With lesions, death primarily from syphilis	70	52.1±0.78
With lesions, death from other cause	49	54.2±1.76
Total	276	52.5±0.81

This generalization is not to be construed as an indication that syphilis has no influence on longevity. The following more detailed

analysis shows that the syphilitic had a shorter life span than the nonsyphilitic, even though no anatomic lesions recognizable as such were found at autopsy (table 21 and chart 8).

The individuals in each group and subgroup were arranged in three age categories under 40, between 40 and 70, and over 7 As was to be expected from our preliminar analysis, control groups A and B were sim larly distributed with respect to these thre age classifications.

TABLE 21.—*Age distribution of white syphilitics and nonsyphilitics in Yale autopsy population*

Group	Age in years									Total	
	20–39 9			40–69 9			70+				
	Number	Percent	V [1]	Number	Percent	V [1]	Number	Percent	V [1]	Number	Percer
Nonsyphilitic:											
Control A	86	24.2	5.2	199	56.0	6.9	70	19.7	4.5	355	100
Control B	84	23.8	5.1	211	59.8	6.8	58	16.4	3.9	353	100
Syphilitic:											
Without lesions	38	24.2	11.7	104	66.2	14.3	15	9.6	5.5	157	100
With lesions, death primarily from syphilis	7	10.0	12.9	57	81.4	21.6	6	8.6	11.2	70	100
With lesions, death from other cause	7	14.2	24.9	37	75.5	37.8	5	10.2	18.7	49	100
Total with lesions	14	11.8	8.7	94	79.0	13.9	11	9.2	7.0	119	100
Total syphilitics	52	18.8	5.5	198	71.7	7.4	26	9.4	3.1	276	100

[1] Variance $= \sigma^2$

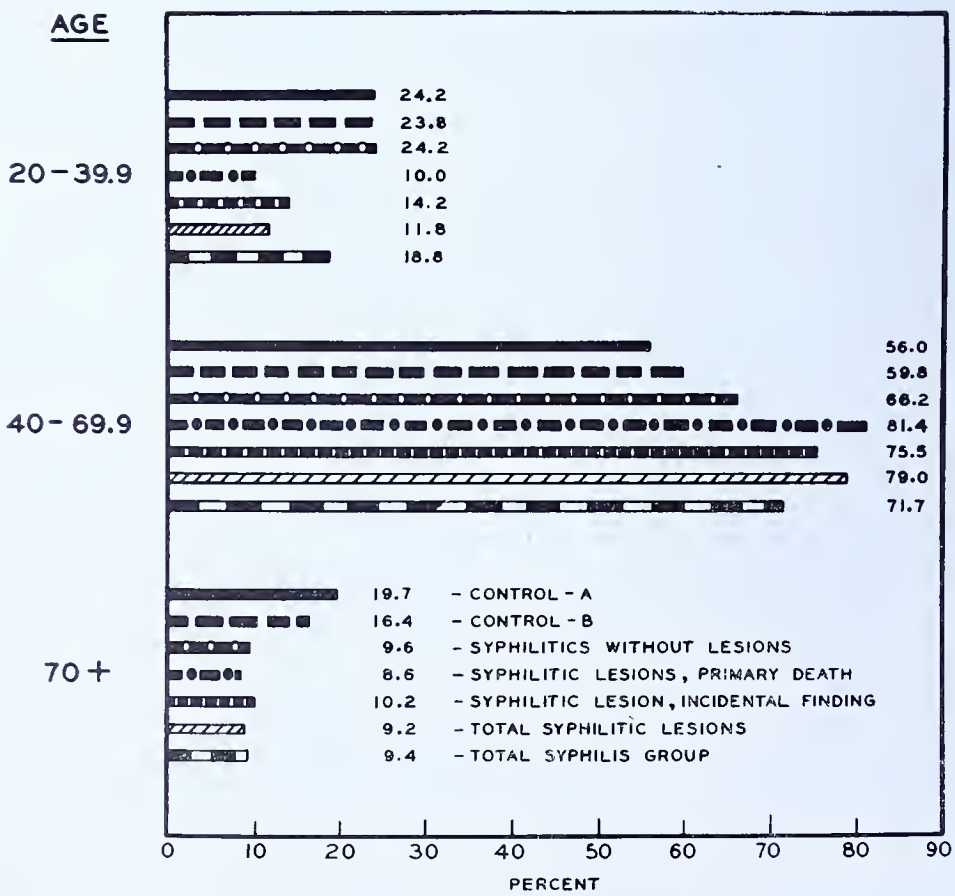

CHART 8.—Age distribution of white syphilitics and nonsyphilitics in Yale autopsy series.

Age 20 to 39.—According to the findings of Vonderlehr and Usilton (*25*), the annual syphilis attack rate per 100,000 persons in 1937 was 1,121 in the age group 20 to 29, and 380 in the age group 30 to 34. Under 20 the attack rate was 299, and over 35 it was 336. The overwhelming majority of primary infections thus occur in the age period 20 to 39. It is generally recognized that a variable number of years must elapse from the time of infection before the tissue changes of late syphilis occur. On this basis one would expect that a group of dead syphilitics with anatomic lesions at autopsy would contain a smaller proportion of individuals in the age group 20 to 39, when most of the primary infections take place, than would be found in a nonsyphilitic population. This expectation is fulfilled by the actual findings. Only 11.8 percent of the deaths among syphilitics with anatomic lesions at autopsy fell into the 20 to 39 year category as compared with the significantly higher values of 24.2 percent and 23.8 percent of the deaths among those comprising the nonsyphilitic populations of control groups A and B. Furthermore, one would expect that the same proportion of a group of syphilitics diagnosed on clinical evidence only, and with no anatomic lesions at autopsy, would succumb in the age group 20 to 39 as in the case of nonsyphilitic persons. This is substantiated by the actual findings, for 24.2 percent of all deaths among the syphilitics who had no recognizable specific lesions at autopsy occurred between 20 and 39, a value which is no different from the comparable values for each of the two control nonsyphilitic populations.

Age 40 to 69.—In the syphilis group the proportion of deaths in the age class 40 to 69 was significantly higher than that observed in either of the two control nonsyphilitic groups. This differential was noted with respect both to the entire group of syphilitics and to the group with anatomic lesions at autopsy. In the case of syphilitics diagnosed clinically and without demonstrable lesions, the proportion dying in this age class was no different from that observed in either control group. More syphilitics succumbed between the ages of 40 and 70 than did nonsyphilitics, although the proportion of syphilitics with no tissue changes and the proportion of nonsyphilitics dying in this age class were no different.

Age over 70.—What proportion of syphilitics and nonsyphilitics lived beyond age 70? There were 19.7 percent and 16.4 percent of control groups A and B in this category in contrast to the significantly lower proportion of 9.4 percent of our total syphilitic group. The break-down by presence or absence of lesions of syphilis is of great interest. It reveals that in our experience, if a syphilitic developed a specific lesion verified by autopsy, and he eventually died primarily as a result of his syphilis, he had the same chances of surviving age 70, about 1 in 10, as the syphilitic with a specific lesion which was not responsible for death. Furthermore, the individual with syphilis, clinically diagnosed and with no anatomic lesion at autopsy, had no greater chance of surviving age 70 than had the syphilitic with demonstrable tissue changes. Each of these syphilitics had about half the chance of the nonsyphilitic of living beyond age 70.

The above findings indicate that syphilis in and of itself definitely reduces longevity. Proportionally more syphilitics with anatomic lesions died between 40 and 69, and fewer survived age 70 than did nonsyphilitics. Only about half as many of the syphilitics who escape tissue changes live beyond age 70 as nonsyphilitics. This latter observation suggests that even though a lesion never develops, or occurs and eventually disappears, the mere fact of infection adversely influences longevity.

Schamberg (*28*) has suggested that our autopsy population contained a number of unrecognized syphilitics who were not included in our syphilis group because of their negative serologic status. Had they been recognized as syphilitic, and included, the disparity between the ratios of nonsyphilitics, and of latent syphilitics in the age group 70 and over would, in Schamberg's opinion, have been equalized. He believes, therefore, that these findings cannot be accepted as indicating that latent syphilis shortens life. The factor mentioned by Schamberg was certainly operative in the selection of our syphilitic group, but it is not possible to estimate the magnitude of its influence on our findings. It is probable, however, that cases of syphilis not included in our syphilis

group because of spontaneous or treatment-induced seronegativity were numerically counterbalanced by cases of latent syphilis who were excluded because their serologic reactions were not studied. As indicated in an earlier chapter, 438 of our original group died at other institutions, and a large majority of these did not have serologic determinations. In addition, 186 died before admission to the New Haven Hospital, and most of these patients had inadequate past histories and laboratory examinations. These 2 groups represent a little more than 10 percent of our total autopsy population, and to them must be added an unknown number of admitted patients who died before serologic tests could be done. We have no way of determining how many seronegative syphilitics were excluded, but by the same token we have no knowledge of the number of seropositive latent syphilitics who were likewise excluded. The 2 groups probably nullified each other.

Evidence from other sources indicates that the disease syphilis does shorten longevity. Smith and M. C. Bruyere (*29*) compared the mortality in a general population with the mortality in that portion of the same population which was known to be syphilitic. Abridged life tables were constructed from available mortality data for whites and Negroes of both sexes. In all four groups considered, the life expectancy of the syphilitic population was lower at every age period than that of the general population. All of the syphilitic persons in this study had received treatment. Heller and P. T. Bruyere (*36*) concluded that the life expectancy of the Negro male between ages 25 and 50, infected with syphilis and untreated, was on the average reduced about 20 percent when compared with nonsyphilitic controls. These two reports, each employing standard statistic methods, emphasize the observation th syphilis, whether treated or untreated, is a sociated with a reduction in longevity.

A revision of the data appearing in tab 4 shows a close parallelism with the Ya material presented in table 21. Table 4, will be recalled, gives the summated distrib tion by sex and decennia of the incidence syphilis in several different autopsy popul tions. The values for males and females given in this table have been combined f comparison with our own material, and a presented in table 22. It will be noted th the two series show remarkably close agre ment when the age distributions of the tw nonsyphilitic populations are contrasted. Th

TABLE 22.—*The age distribution of nonsyphilitic persons and of syphilitic persons with anatomic lesions, in two different autopsy populations*

Group	Source of data	Age in years						Total	
		20–39.9		40–69.9		70+			
		Number	Percent	Number	Percent	Number	Percent	Number	Percen
Nonsyphilitic	Yale series	170	24.0	410	57.9	128	18.1	708	100.
	Table 4	9,073	23.2	22,699	58.1	7,265	18.7	39,037	100.
Syphilitic with lesions	Yale series	14	11.8	94	79.0	11	9.2	119	100.
	Table 4	278	16.4	1,292	76.4	122	7.2	1,692	100.

agreement is further emphasized by the para lelism observed in the age distribution of th syphilitic groups in both series. The com parative ratios in none of the categories we significantly different. Here again it is see that although about 20 percent of the no syphilitic population survived age 70, le than 10 percent of the syphilitic group each of the two series lived to age 70 more. This confirmation of our own findin by the summated experience of five differe investigators lends added weight to the co clusion that syphilis decreases longevity.

Several questions immediately come mind. Does syphilis increase susceptibili to other mortal diseases? Or are syphilitics a class constitutionally susceptible to oth diseases? Or perhaps the environmental i fluences which contributed to the probabili of acquiring syphilis in the first place a also such as to have an adverse influence o longevity? Schamberg (*28*) has recently cite evidence in support of the latter hypothesi

THE RELATION BETWEEN BLOOD SEROLOGIC TESTS AND ANATOMIC LESIONS AT AUTOPSY [1]

Major energies in the field of serodiagnosis have been concentrated on technics, evaluation studies, and population surveys, while only minimal efforts have been directed to elucidating the relationship between blood serologic tests and organic lesions of syphilis. It is no doubt of great value to ascertain that a certain proportion of a given population has serologic positivity when tested by a technic with known ratings for sensitivity and specificity. Of greater significance, however, is the projection of this information into terms of morbidity and mortality. What proportion of individuals with positive serologic tests as the only indication of infection can be expected to show organic lesions or to develop them in the future, and what is the probability that these changes will be primarily responsible for death? Furthermore, what proportion of those with a clinical history of syphilis and negative serologic tests can be expected to harbor the infection and to die therefrom? When serologic reversal has occurred, either spontaneously or following specific therapy, what is the expectation that organic lesions, if present, will completely regress leaving no evidence of their previous existence? When serologic reversal does not take place in spite of persistent therapy, what is the probability that organic lesions will persist and cause incapacitating illness and death?

These are problems of far-reaching importance in the interpretation of serologic data, but they have received little attention in the past. They can be approached primarily through retrospective studies of autopsy data, and this report represents such an approach. It is unfortunate that many aspects of the general problem cannot be clarified by our basic observations, which are limited in numbers, but certain generalizations from our data are nevertheless tenable. These will be emphasized in subsequent paragraphs.

During the entire period of this survey all serologic examinations on patients admitted to the New Haven Hospital were carried out in a central serologic laboratory under the supervision of the Department of Immunology. Prior to 1925 the tests were performed by graduate students; since 1925 salaried technicians have been employed. A modified Kolmer complement-fixation test has been the standard procedure. In 1928 the Kahn precipitation test became routine, checked where indicated by the complement-fixation test. The Kline exclusion and diagnostic tests have been used on occasion.

This review is not concerned with the evaluation of serologic performance and the results are not intended to champion any test or tests. For this reason the data have been analyzed without regard to particular serologic procedures. Cases have been classified as serologically positive when any one test has been positive even though one or more other serologic procedures during the same admission were negative.

The Relation Between Serologic Tests and Anatomic Lesions

Table 23 is an association table showing the relation between positive and negative serologic tests in syphilitic individuals with and without anatomic lesions at autopsy. It summarizes the serologic determinations during the last admission of each of the 380 individuals comprising our material. In all subsequent discussions the 4 "doubtful" cases

[1]This chapter revises the article *Studies in Syphilis. IV. The Relation Between Blood Serologic Tests and Anatomic Lesions at Autopsy*, by Bernard Black-Schaffer and Paul D. Rosahn, which was published in the *American Journal of Syphilis, Gonorrhea & Venereal Diseases*, vol. 28, p. 27, 1944.

TABLE 23.—*The serologic results of 380 syphilitics related to the presence or absence of anatomic lesions at autopsy*

Serologic results	Anatomic lesions at autopsy					
	Number			Percent		
	Present	Absent	Total	Present	Absent	Total
Positive	87	110	197	44.2	55.8	100.0
Negative ...	31	85	116	26.7	73.3	100.0
Subtotal ..	118	195	313	37.7	62.3	100.0
Doubtful....	3	1	4	75.0	25.0	100.0
Not known.	35	28	63	55.6	44.4	100.0
Total...	156	224	380	41.1	58.9	100.0

are excluded from consideration. Of the 63 individuals with no reported serologic studies, 19 were positive, 7 were negative, and 1 was doubtful on examination of blood obtained post mortem. Thus 36 of our group of 380 had no serologic examination on their last admission or at necropsy.

It is noteworthy that all evaluation studies give higher ratings for specificity than for sensitivity. Sensitivity may be defined as the ability of a test to detect the presence of the reacting substance in the serums of known syphilitics; and specificity may be said to indicate the ability to exclude the presence of reagin in the serums of presumably nonsyphilitic donors. In many instances tests have been 100 percent specific, while a rating of 90 percent or more for sensitivity is exceptionally fine. In other words, false negative reports are much more frequent than false positive findings. In spite of this it is more usual for physicians to request confirmatory tests when a positive report is rendered than when a negative finding is reported.

The frequency of post-mortem lesions in individuals with ante-mortem positive serologic tests was significantly greater than in syphilitics with ante-mortem negative tests. Of 197 individuals with positive blood tests, 87 (44.2 $\pm$ 3.54 percent) had anatomic lesions, while of 116 syphilitic patients with negative serologic tests, 31 (26.7 $\pm$ 4.11 percent) had lesions. The difference between these values is significant (D $=$ 17.4 $\pm$ 5.42, t $=$ 3.2; chi-square $=$ 9.4528, n $=$ 1, P $=$ 0.0021). It is noteworthy, however, that among those whose ante-mortem serologic tests were unknown or doubtful, the proportion of post-mortem lesions found was significantly higher than among thos whose blood tests were known, and that i actual percentages this unknown group ha by far the highest proportion of lesions. Th is probably because many of the individua in this group were selected by the very fa that lesions were present at autopsy.

The Serologic Tests of Individuals with Anatomic Lesions

Table 24 summates the serologic finding in 826 individuals who presented anatomi lesions of syphilis at autopsy on the basis c criteria acceptable to the different reporter

TABLE 24.—*The serologic tests of individua with anatomic lesions of syphilis at autops according to various authors*

Author	Serologic results					
	Number			Percent		
	Positive	Negative	Total	Positive	Negative	Tot
Yale series..	87	31	118	73.7	26.3	100
Brines (*31*).	321	82	403	79.7	20.3	100
Melchior (*19*)	82	31	113	72.6	27.4	100
Symmers (*11*)	46	21	67	68.7	31.3	100
Teodori (*17*)	103	22	125	82.4	17.6	100
Total...	639	187	826	77.4	22.6	100

[1] Figures in parentheses are bibliographic references

It should be remembered that there exists n uniformity as regards serologic procedure or criteria of anatomic changes of syphilis a between the several investigators. The Yal material and Melchior's (*19*) contributio are based on individuals aged 20 and ove Teodori's (*17*) findings do not include neo natal syphilitics, nor individuals with negativ serologic tests and a history of antisyphiliti therapy in the recent past. This latter pro cedure obviously gives increased weight t the group with positive serologic tests. Th ages of Symmers' (*11*) and Brines' (*31* cases do not appear in their original report However, congenital syphilitics were exclude from Symmers' findings as far as practicable and from internal evidence it is fair to as sume that only an insignificant fraction o Brines' autopsy population of syphilitics rep resents neonatal infections. Brines' observa tions include 21 individuals with doubtfu serologic reports, and our own material ha 3 cases in this category; these have been ex cluded from the table. In spite of variation

in technics and criteria it is seen that approximately one-quarter of these individuals with anatomic lesions at autopsy were reported to have been serologically negative. This is not to be interpreted as indicating persistent negativity, for it is entirely reasonable to assume that serologic positivity might have been discovered in many of these individuals had they been tested on other occasions. In this connection, it is of interest that 7 of our 31 patients with negative serologic tests on their last admission and anatomic lesions of syphilis at autopsy are known to have been serologically positive on a previous occasion. However, the findings do suggest that a spot survey of individuals with anatomic lesions of syphilis, without regard to duration of infection, types of lesions, or kinds or amounts of treatment, will disclose serologic negativity in about one-fourth of the group. Even though an anatomically demonstrable syphilitic lesion is present, the blood serums of these individuals do not react positively to the usual serologic tests for syphilis.

The explanation for this phenomenon is not readily apparent. Possible variables which may have some relation to it are: duration of infection; anatomic distribution of lesions; the presence of single or multiple systemic disease; and treatment status. Each of these will be considered separately by comparing the negative serologic group with the positive group, both groups having syphilitic lesions at autopsy.

Variables Which May be Responsible for Serologic Negativity in the Presence of Anatomic Lesions of Syphilis

Duration of Infection

Information concerning the duration of infection was available for only 8 of the 31 individuals with negative serologic tests, and for 24 of the 87 with positive tests. Six of the 8 in the first group, and 20 of the 24 in the second had had their infections for more than 15 years. There is no significant difference between these values, although the observations are admittedly too few for final conclusions.

Anatomic Distribution of Lesions

The distribution of the anatomic lesions in the 118 patients with anatomic lesions and known serologic tests is shown in table 25.

TABLE 25. — *Systemic distribution of anatomic lesions at autopsy in individuals with positive and negative serologic tests on their last admission*

System	Serologic tests		
	Positive	Negative	Total
Cardiovascular	72	26	98
Central nervous	17	4	21
Liver	8	2	10
Other	4	1	5
Total	[1] 101	[2] 33	134

[1] 87 different patients.
[2] 31 different patients

The incidence of cardiovascular disease in this group was 83.1 percent; of central nervous system syphilis, 17.8 percent; and of liver syphilis, 8.5 percent. The comparable figures reported by Brines are 71.4 percent, 30.6 percent, and 6.2 percent. In our group of 31 patients with negative serologic tests, 26 (83.9 percent) had cardiovascular syphilis; 4 (12.9 percent) had syphilis of the central nervous system; and 2 (6.5 percent) showed liver changes of syphilis. In comparison with these findings, 72 (82.8 percent) of 87 patients with positive serologic tests had cardiovascular syphilis; 17 (19.5 percent) had central nervous system syphilis; and 8 (9.2 percent) had syphilitic livers. There is no significant difference between the negative and positive serologic groups as regards the distribution of anatomic lesions, and it is not possible, therefore, to explain on this basis the negative serologic results in individuals with anatomic lesions.

Syphilis of One or of More Than One System

Brines has reported that individuals with lesions in more than one organ had a higher incidence of positive serologic tests than those in whom only one organ was the locus of syphilitic disease. Our own data have been analyzed by system rather than by organ. The positive serologic group of 87 included 14 (16.1 percent) with lesions in more than one system, as contrasted with 2 individuals

(6.5 percent) in our group of 31 with negative serologic tests. Although these values appear to confirm Brines' findings, the difference between them is statistically not significant. However, the results are suggestive, and further observations on this aspect of the problem seem warranted.

Treatment

The treatment status is known of 75 of our 87 patients with positive serologic tests and anatomic lesions at autopsy. There were 57 patients in this group (76 percent) who had never received any specific therapy. Our negative serologic group of 31 included 25 whose treatment status was recorded. Of this group 18 (72 percent) were never treated. The two groups are thus no different from each other so far as therapy is concerned.

In summary of the above discussion, we have no indication that duration of infection, system or systems involved, or therapy was individually responsible for negative serologic tests in the presence of an anatomic lesion of syphilis. There is suggestive evidence that when a single system is involved, the serologic results are more likely to be negative than when more than one organ system is the site of syphilitic change. Final conclusions on any of these factors should not be drawn, however, because of the limited number of observations.

Scott (32) has suggested that perhaps the negative serologic results in syphilitics with anatomic lesions were in large measure a reflection of the insensitive serologic technics employed in the early years of this autopsy series. The material has been analyzed with this possibility in mind. Of the 118 syphilitics with anatomic lesions, 38 were autopsied in the period 1917 to 1927, and 80 between 1928 and 1941. Seven of the former group, or 18.4 percent, were serologically negative on their last admission, as contrasted with 24, or 30 percent of those autopsied in the later time period. These two values are not significantly different, although the direction and magnitude of their difference tend to substantiate Scott's hypothesis. With the limited number of observations available for analysis, however, it can be concluded that the frequency of negative serologic results in the presence of anatomic lesions of syphilis was not significantly influenced by any lack of sensitivity that mig have existed in the early serologic procedur

Anatomic Lesions in Individuals with Positive Serologic Tests

In table 26 is shown the presence or a sence of anatomic lesions of syphilis in in viduals with ante-mortem positive serolog tests. Four individuals with doubtful tests our material have been excluded. With o exception, Melchior, all of the reporters fi an approximately equal division into tho with and those without specific anatom changes. The reasons for the disparity b tween Melchior's observations and those the others are not readily apparent. The sur mated total, however, indicates that 223 i

TABLE 26.—*The presence or absence of an tomic lesions at autopsy in individuals wi positive serologic tests, according to vario authors*

Author	Anatomic lesions at autopsy					
	Number			Percent		
	Present	Absent	Total	Present	Absent	Tot
Yale series	87	110	197	44.2	55.8	10
Brines	39	45	84	46.4	53.6	10
Melchior	82	17	99	82.8	17.2	10
Symmers	45	51	96	46.9	53.1	10
Total	253	223	476	53.2	46.8	10

dividuals (46.8 percent) of the 476 wi positive serologic tests revealed no anatom changes at autopsy consistent with a dia nosis of syphilis. The conclusion is inevitab that the toss of a coin would have been effective in indicating which of the cas would show anatomic evidence of the disease. Serologic positivity in and of itse is thus uncertain evidence of the tissu changes of syphilis as determined by autops examination.

Variables Which May Be Responsible for Serologic Positivity in the Absence of Anatomic Lesions of Syphilis

There are at least two factors which ma account for the absence of anatomic lesion in individuals with positive serologic test These are duration of infection, and therapy

Duration of Infection

This was known for 24 of our 87 patients with positive serologic results and anatomic lesions. Infection was known to have been present for more than 15 years in 20 of these individuals. In contrast to these findings, of 16 patients with positive serologic tests and no anatomic lesions at autopsy, the duration of whose infection was known, 10 had evidence of the disease for more than 15 years. There is no significant difference between these two groups so far as duration of infection is concerned.

Specific Therapy

We have information concerning the therapy received by 75 of the 87 patients with positive serologic tests and anatomic lesions at autopsy, and by 90 of the 110 individuals with positive tests and no anatomic lesions. In the first group mentioned, 57 (76.0 percent) never received any treatment, compared to 72 (80.0 percent) in the second group. Here again there is no significant difference between the two series. It is noteworthy that approximately three-quarters of our cases with positive serologic tests never received specific therapy of any kind.

Relation Between Clinical Status and Lesions at Autopsy in Individuals with Positive Serologic Tests

There were 197 individuals with antemortem positively reacting serums in our series of 380 syphilitics. These were grouped in two distinct clinical categories as shown in table 27. The first consisted of those with latent syphilis, a positive serologic result being the only clinical evidence of the disease. The second group comprised individuals with clinically diagnosed anatomic lesions, usually of the cardiovascular or central nervous systems. A clinical diagnosis of an anatomic lesion was made in 62 of 87 individuals (71.3 percent) with demonstrable tissue changes at autopsy, and in 18, or 16.4 percent, of 110 individuals with no morphologic lesions at autopsy. The difference between these values is highly significant. Thus among patients with anatomic lesions at autopsy, the clinical diagnosis of organic disease was made more frequently than among patients with no autopsy changes. Analysis of table 27 along the horizontal rows instead of the vertical rows, shows that 62 of 80 patients (77.5 percent) in whom a clinical diagnosis of organic lesions was made, had anatomic changes at autopsy, as compared with only 25 of 117 patients (21.4 percent) who were diagnosed clinically as latent syphilitics. Seven of these 25 patients incorrectly diagnosed as latent syphilitics died as a direct result of syphilitic lesions. This is 6.0 percent of the 117 cases of clinically diagnosed latent syphilis.

TABLE 27.—*The clinical status on the last admission of 197 individuals with positive serologic tests, related to the presence or absence of anatomic lesions at autopsy*

Clinical status	Anatomic lesions					
	Number			Percent		
	Present	Absent	Total	Present	Absent	Total
Latent—no clinically apparent organic lesions	25	92	117	28.7	83.6	59.4
Organic lesions clinically diagnosed....	62	18	80	71.3	16.4	40.6
Total..	87	110	197	100.0	100.0	100.0

A comparison of these results with those of the previous section indicates the value of clinical study in determining the significance of a positive serum. When the only information available about a patient was the fact that his serum was positive, the probability that he had an anatomic lesion was about 50 percent. If, however, to this knowledge was added that derived through clinical examination, the chances of correctly diagnosing an anatomic lesion were increased to about 75 percent. A clinical appraisal thus brought the probability of correctly diagnosing an organic lesion out of the realm of coin-tossing. It should be pointed out that the above analysis does not deal with the accuracy of the clinical diagnosis of organic syphilitic disease, but rather is concerned with the confirmation of the clinical diagnosis of an anatomic lesion by the presence of any syphilitic lesion at autopsy.

Relation Between Clinical Status and Lesions at Autopsy in Syphilitic Individuals with Negative Serologic Tests

Table 28 summarizes the clinical status of 116 syphilitic individuals with negative serologic tests on their last admission in relation to the presence or absence of anatomic lesions at autopsy. In this group were 43 patients who on clinical grounds were believed to have been cured; at autopsy, lesions were found in 5 (11.6 ± 4.87 percent). Of 29 patients who on clinical grounds were believed to have an organic syphilitic lesion, 8 were found at autopsy to have morphologic tissue changes of syphilis. In this instance the ante-mortem diagnosis was correct in 27.6 ± 8.3 percent. The difference between these two values is not significant. Lesions were found at autopsy just as often in those clinically diagnosed "cured" as in those clinically diagnosed "organic disease." The conclusion appears warranted that, given a syphilitic individual with negative serologic tests, a clinical evaluation leading to the specifically stated impression of "no anatomic lesion" or "cured" was likely to be no more accurate when checked with findings at autopsy than a clinical diagnosis of organic disease.

It will be noted that table 28 includes a third category of patients classified on clinical evidence, the "undiagnosed." These comprised 44 of our 116 syphilitic patients (37.9 percent) with negative serologic tests. Five of this group had a previous history of a positively reacting serum which was either ignored or overlooked by the examining physician, 17 had anatomic lesions at autopsy which were not diagnosed clinically, and had significant anamneses or other evide which justified their inclusion in the grou syphilitics. This procedure merits further planation. In 5 of these 22 patients the p mortem serologic tests were strongly posit one other had a positive complement-fixa test on the spinal fluid, not emphasized the clinical appraisal, and 16 gave a stor primary lesions which clinically were ei ignored or overlooked. Only one of thes received treatment, while the remaining patients represent those included in the sy ilis group solely on the basis of a histor a primary lesion. Herein may lie a sourc error, for proof is lacking that the ger sore mentioned by these 15 patients in t anamneses was actually a syphilitic lesion it were, healing without residual tissue d age occurred in the absence of spe therapy.

The conclusion that, among syphilitics v negative serologic tests, the clinical diagn of latency was no more accurate than clinical impression of organic involvemen of interest when compared with the findi on patients with positive blood tests. clinical impression of no anatomic lesion the presence of positive tests was correct 92 of 117 cases (78.6 percent), whil similar impression in the presence of nega serologic tests was correct in 64 of 87 c (73.6 percent). These values do not di from each other. In contrast to this ag ment are the findings among individuals whom a clinical diagnosis of organic invo ment was made. In this instance the diagn was correct in 62 of 80 cases with posi serologic tests (77.5 percent), as compa

TABLE 28.—*The clinical status on the last admission of 116 syphilitics with negative serologic tests, related to the presence or absence of anatomic lesions at autopsy*

Clinical status	Anatomic lesions at autopsy						To
	Present			Absent			
	Serologic test negative but previously positive	Serologic test negative	Subtotal	Serologic test negative but previously positive	Serologic test negative	Subtotal	
Cured	3	2	5	22	16	38	
Organic disease clinically diagnosed	3	5	8	10	11	21	
Syphilis not diagnosed	1	17	18	4	22	26	
Total	7	24	31	36	49	85	

with a confirmed clinical diagnosis in 8 of 29 patients with negative blood tests (27.6 percent). These latter values are significantly different. They indicate that when a clinical diagnosis of organic lesions had been made, anatomic confirmation at autopsy was found more often when the serologic test was positive than when it was negative, but when a clinical diagnosis of no organic involvement was recorded, autopsy lesions were found just as often among those whose tests were negative as among those whose tests were positive.

It is apparent that more than usual clinical scrutiny must be followed before making a clinical diagnosis of an organic lesion in the presence of a negative serologic test for syphilis. This is shown by the fact that among those having positive tests, autopsy lesions were found in 62 of 80 (77.5 percent) in whom the diagnosis was made clinically, but lesions at autopsy were noted in only 25 of 117 (21.4 percent) in whom the clinical diagnosis of organic lesions was not made. The difference between these is significant and chi-square equals 60.7098. On the other hand, among those with negative blood tests before death, autopsy lesions were found just as often when the clinical diagnosis had not been made as when it had, the former percentage being 11.6 (5 out of 43) and the latter 27.6 (8 out of 29). Chi-square in this case is 2.9811, which is not significant.

Incidence of Positive Serologic Tests in Syphilitics Dying Primarily of Syphilis and in Those with Syphilitic Organic Disease An Incidental Finding at Autopsy

Of 66 individuals who died primarily of syphilitic organic disease 54 (81.8 $\pm$ 4.87 percent) had positive ante-mortem serums while the balance had negative blood tests. There were 52 patients in whom syphilitic organic disease was observed at autopsy as only an incidental finding unrelated to the cause of death. Of this group, 33 (63.5 $\pm$ 6.68 percent) had positive serums ante mortem. The difference between these two groups is probably significant ($D = 18.3 \pm 8.26$, $t = 2.21$, $P < 0.05$). A previous section has indicated that the frequency of positive serologic tests among 195 individuals with historical or other evidence of syphilis but with no anatomic changes produced by the disease was 110 or 56.4 $\pm$ 3.55 percent. This is statistically no different from the above-indicated 63.5 percent frequency of positive serums in syphilitics with incidental organic lesions unrelated to the cause of death, but has a highly significant difference from the 81.8 percent incidence of positive serologic tests in individuals dying primarily from syphilitic organic disease. ($D = 25.4 \pm 6.02$, $t = 4.21$, $P < 0.01$). However, of the three groups, the one in which syphilitic lesions were primarily responsible for death had the highest incidence and the group with no lesions had the lowest incidence of positive blood tests. This suggests that there is an increasing proportion of positive serologic tests with increasing activity of the disease.

Syphilis as a Primary Cause of Death in Syphilitics with Positive and Negative Serologic Tests

There were 197 individuals with positive serologic tests in our series. Syphilitic organic lesions were primarily responsible for the death of 54 of these, a frequency of 27.4 $\pm$ 3.17 percent. In contrast to this finding, 12 individuals in our group of 116 with negative serologic tests died primarily as a result of the morphologic tissue changes of syphilis, a rate of 10.3 $\pm$ 2.82 percent. The difference between these two values is highly significant. In general terms, about 1 out of 4 syphilitics with positive serologic tests, and about 1 out of 10 syphilitics with negative tests, died primarily as a result of their infection. The likelihood of syphilis being the primary cause of death was more than twice as great in individuals with positive blood tests as in syphilitics with negative serums.

Serologic Reversal in Relation to Anatomic Lesions

Forty-three individuals whose serologic tests were negative on their last admission were known to have had a previously positive serum. This represents 37.1 percent of all the negative reactions. Anatomic lesions were observed in 7 of the 43, or 16.3 percent. Four of these were males and 3 were females. Of the males, only 1 had not been treated, and

this person died primarily of syphilitic disease. Of the females, 2 had received no treatment and none died as a direct result of syphilis. Anatomic lesions were completely absent in 36 individuals, 15 males and 21 females. Of the males without anatomic lesions, 6 never received treatment, and of the females, 8 were not treated. These observations are admittedly too few for generalizations, but they appear to indicate that neither of the two variables, sex or therapy, was a factor which could account for the presence or absence of anatomic lesions at autopsy in individuals with serologic reversal. More reliance can be placed on the finding that anatomic changes were noted at autopsy in about 1 out of 6 such cases. Of doubtful value is the observation that 1 out of 43 individuals with serologic reversal died directly as a result of syphilitic tissue changes.

Sex, Serologic Tests, and Anatomic Lesions of Syphilis

In table 29 is shown the distribution by sex and serologic results of 118 persons with anatomic lesions at autopsy. It is evident that an equal proportion, approximately three-quarters, of both males and females with anatomic lesions had positively reacting serums. Tables 30 and 31 classify all cases

TABLE 29.—*The sex and serologic results of individuals with anatomic lesions of syphilis at autopsy*

Sex	Serologic results					
	Number			Percent		
	Positive	Negative	Total	Positive	Negative	Total
Male	66	23	89	74.2	25.8	100.0
Female	21	8	29	72.4	27.6	100.0
Total	87	31	118	73.7	26.3	100.0

with positive and negative serologic tests according to sex and syphilitic lesions as a primary cause of death, as an incidental finding, or as absent at autopsy. Neither in the group with positive serologic tests nor in that with negative tests is there any significant difference between the sexes as regards any of these categories. Of the 197 cases with positive tests, 136 (69.0 percent) were males, compared with 78 males (67.2 percent) of 116 syphilitics with negative blood

TABLE 30.—*The sex and primary cause death in syphilitic individuals with posi serologic tests*

Primary cause of death	Sex					
	Number			Percent		
	Male	Female	Total	Male	Female	T
Syphilis	40	14	54	29.4	23.0	
Other than syphilis, but syphilitic lesions found at autopsy	25	8	33	18.4	13.1	
Other than syphilis, and syphilitic lesions not found at autopsy	71	39	110	52.2	63.9	
Total	136	61	197	100.0	100.0	1

tests. These values likewise are not sign cantly different. It appears, therefore, that did not influence the incidence of positive negative serologic tests among individu with anatomic lesions at autopsy, or the quency of syphilitic lesions as a primary ca of death among syphilitics with positive negative blood tests. This homogeneity tween the sexes suggests that the observati and conclusions in the earlier sections of t report apply with equal merit both to ma and to females.

TABLE 31.—*The sex and primary cause death in syphilitic individuals with negat serologic tests*

Primary cause of death	Sex					
	Number			Percent		
	Male	Female	Total	Male	Female	T
Syphilis	8	4	12	10.3	10.5	
Other than syphilis, but syphilitic lesions found at autopsy	15	4	19	19.2	10.5	
Other than syphilis, and syphilitic lesions not found at autopsy	55	30	85	70.5	79.0	
Total	78	38	116	100.0	100.0	1

Anatomic Lesions in Treated Syphilitics with Positive Serologic Tests

The 197 syphilitics with positive serolo results on their last admission included patients who had received variable amou of arsenicals during the course of th

disease. In spite of this therapy, serologic reversal failed to take place, as indicated by their positively reacting serums on their last hospital admission. Eighteen of this group (50 percent) had anatomic lesions of syphilis at autopsy, and 9, or one-quarter, died primarily as a result of these lesions. The series is obviously too small for generalizations and none will be attempted.

General Discussion

The findings reported herein should be interpreted in the light of three basic considerations. In the first place a discussion of the relation between any variable, blood serologic tests in this instance, and anatomic tissue changes of syphilis at autopsy, should be prefaced by a clear statement of the criteria followed in diagnosing tissue alteration as evidence of syphilitic disease. Such a statement was given in a previous chapter and merits repetition here: "All diagnoses were based upon gross and microscopic examinations and all were checked and confirmed by group discussion among members of the Department at the time of the necropsy. The criteria generally observed were those enunciated by Nickel (*21*), that is, definite anatomic changes of syphilis of the central nervous system, vascular tree, bone, and parenchymatous organs including liver. Presumptive evidence of syphilis such as orchitis fibrosa, lingua glabia, and so-called syphilitic cirrhosis of the liver were not accepted as indicative of morphologic syphilis. Warthin's (*5*) criteria of lymphocytic and round cell infiltration in liver, heart, adrenals, testes, and pancreas were not followed."

Secondly, our basic data are incomplete because an examination of the central nervous system was not conducted in every case. This is a particularly serious deficiency, especially with regard to the 195 cases with known serologic tests and no anatomic evidence of syphilis. Of this group, 123 (63.1 percent) had an examination of the brain or spinal cord or both at necropsy. The presence or absence of morphologic changes in the central nervous system of the remaining 72 is not known, and to this extent our conclusions must be viewed with caution.

The third factor which must be kept in mind in the interpretation of our data is concerned with the size of our sample. In any statistical study such as ours, where relatively small samples are employed, the demonstration of statistically significant differences between compared groups is much more reliable than the demonstration that compared groups are homogeneous. Especial caution must be exercised in drawing conclusions from samples which are obviously too small and therefore may not be representative of the population from which they were drawn. For this reason the present study is of limited value as regards such special aspects of the general problem as the role of therapy, or the frequency of anatomic changes of syphilis in cases of serologic reversal, or in treated syphilitics with persistently positive blood tests. Moreover, our observations are too few to permit of break-down into age and sex and race categories. Only the accumulated and pooled experience of several institutions comparable to our own will provide sufficient material for acceptable generalizations on such problems.

FIBROSIS AND ROUND CELL INFILTRATION OF THE PARENCHYMATOUS ORGANS (WARTHIN) IN RELATION TO SERODIAGNOSTIC FINDINGS [1]

The tissue changes which Warthin believed were pathognomonic of syphilitic infection have been discussed in chapter 4. In pursuance of the general problem of the specificity of these lesions, it appeared advisable to study their relation to the results of serologic tests for syphilis.

Material and Methods

The comparisons to be presented are between two groups, one composed of individuals with positive serums, and the other of syphilitic persons with negative serums. Table 32 gives the sex distribution of the two groups according to the presence or absence

TABLE 32.—*Distribution of 225 syphilitic patients according to sex, serologic status, and presence or absence of anatomic lesions of syphilis at autopsy*

Serologic test for syphilis	Anatomic lesions present		Anatomic lesions absent		Total
	Male	Female	Male	Female	
Positive	50	17	49	26	142
Negative	19	3	38	23	83
Total	69	20	87	49	225

of anatomic lesions of syphilis at autopsy. Each of the 61 individuals with seronegative reactions in whom anatomic lesions of syphilis were absent at autopsy was diagnosed as syphilitic on good clinical or historical evidence, and 22 (36.1 percent) were known to have reacted positively to an earlier serologic test for syphilis. All were white persons, years of age or older. A detailed descript of the microscopic technic and of the tis alterations denoted "Warthin lesions" been presented in chapter 4.

The serologic tests were performed in central laboratory, employing technics wh have been described in chapter 6. The c square test of homogeneity has been utiliz in the statistical comparisons, and significan has been attached to values of $P \leq 0.01$

Results

Table 33 gives the distribution of Wart lesions according to the organ involved a to serologic classification. In none of the organs under consideration was the freque of Warthin lesions in the serologic posit group significantly different from the co sponding frequency of these lesions in serologic negative group. Thus the serolo results in syphilitic individuals with without frank anatomic evidence of disease were not influenced by the tis changes described by Warthin.

TABLE 33.—*Distribution of Warthin lesi among syphilitic persons with positive negative serologic reactions, according t organs*

Organ involved	Serologic test for syphilis	Number of cases	Warthin lesion present	Chi-sc
Heart	Positive	113	48	
	Negative	71	20	
Pancreas	Positive	102	44	
	Negative	62	30	
Adrenal	Positive	70	24	
	Negative	75	23	
Liver	Positive	119	44	
	Negative	69	20	
Testis	Positive	35	18	
	Negative	26	14	

[1] This chapter revises the article *Studies in Syphilis. VI. Fibrosis and Round Cell Infiltration of the Parenchymatous Organs (Warthin) in Relation to Serodiagnostic Findings,* by Paul D. Rosahn, which was published in the *Journal of Venereal Disease Information,* vol. 27, p. 126, 1946.

In the above analysis, syphilitic persons with and without anatomic lesions of syphilis at autopsy were grouped together. In order to eliminate any possible distortion of the results that might have occurred because of the inclusion in the analysis of syphilitic persons with frank anatomic lesions, a similar analysis was conducted on the group consisting of 136 individuals (see table 32) in whom no evidence of syphilis was discovered post mortem. The results are shown in table 34. Here again the frequency of Warthin lesions in syphilitic individuals with positively reacting serums was organ for organ no different from the frequency of these lesions in those with negative serums.

TABLE 34.—*Distribution of Warthin lesions among syphilitic persons with no anatomic evidence of syphilis at autopsy, according to organs and to serologic reaction*

Organ involved	Serologic test for syphilis	Number of cases	Warthin lesion present	Chi-square
Heart	Positive	57	22	1.51
	Negative	51	14	
Pancreas	Positive	51	25	0.13
	Negative	42	19	
Adrenal	Positive	25	7	0.17
	Negative	60	16	
Liver	Positive	65	27	1.43
	Negative	49	15	
Testis	Positive	15	9	0.02
	Negative	16	10	

The preceding comparisons have to do with the presence or absence of Warthin changes in single organs as related to the results of serodiagnostic tests. An extension of this study was made to determine whether the multiplicity of organs showing Warthin changes could be related to the results of serologic tests for syphilis. For this purpose, the autopsy protocol of each of the 225 syphilitic individuals was reviewed, and a tabulation was made of the number of organs showing the Warthin changes. There were 109 persons in the group with positively reacting serums in whom three or more organs were examined for Warthin changes, as contrasted with 67 persons in the group with negative serodiagnostic findings. Fifty-one of the first group and 31 of the second showed Warthin changes in two or more organs. There is no significant difference between these findings (chi-square = 0.00+). Thus the number of parenchymatous organs showing Warthin changes was not related to the results of serologic tests for syphilis.

On the basis of these comparisons it can be concluded that there is no correlation between the tissue changes described by Warthin, and the reaction of the serum to known tests for syphilis.

THE END RESULTS OF UNTREATED SYPHILIS [1]

The 380 patients with syphilitic disease who were studied at autopsy and who form the basis for this series of reports, received varying amounts of antisyphilitic therapy. Some were well treated by modern standards, others received minimal amounts of treatment, and the third group was untreated. A study of this latter group has presented the opportunity to determine the distribution of morphologic lesions of syphilis in an untreated syphilitic population. This report will present these findings. In only two other series, those of Bruusgaard and of the United States Public Health Service, has there been any attempt to evaluate the clinical and postmortem evidence of syphilis in patients who received no specific therapy for their disease. The work of these investigators is noteworthy and warrants further comment.

In 1929 Bruusgaard (*33*) published a classic report on the fate of syphilitic patients who had received no specific therapy. This study was made on the basis of material which, to quote Bruusgaard's words, "is hardly to be duplicated anywhere else." During the period 1889 to 1910 neither potassium iodide nor mercury was employed in the treatment of early syphilis at C. Boeck's clinic at the University of Oslo. Boeck believed that these drugs do not cure the disease but disturb the healing forces of the body. Consequently the disease becomes atypical and results in serious late lesions, especially of the central nervous system. In the period mentioned, 2,181 patients with primary and secondary syphilis were seen, of whom 1,388 were women and 793 were men. Potassium iodide was occasionally given but never in larger quantities than 100 to 200 grains, and mercury ointments were employed in very few cases. For all practical purposes the gr was untreated.

Bruusgaard began his personal intervi of these patients in 1924 and completed th in 1927, including in his study only th patients originally seen from 1891 to 19 He was able to trace 309 living patients fr this group, and these were thoroughly exa ined clinically. All received a complete neu logic examination and X-ray studies of heart. In certain instances a spinal fl examination was performed and almost patients had a blood Wassermann study. formation about paretics and tabetics was tained from hospitals and asylums. To t group of 309 living patients there w added 164 patients who had died of kno cause, and 40 on whom autopsies had be performed. The findings he presented in series of tables which have been summariz by Moore (*34*) and by Sowder (*35*), a are presented in somewhat different form tables 35 and 36. Any discrepancy betwe the data as presented in these tables a those published by the above-mention authors arises from differing classificati of Bruusgaard's published findings. Th discrepancies are not serious, however, a do not alter the general conclusions. As in cated in table 36, only 23.0 percent of entire group presented clinical or autop evidence of involvement of the cent nervous system, of the cardiovascular syste or died of syphilitic disease. An additio 12.2 percent showed the less serious syphili tissue changes in skin or bone. The maining group, comprising 64.8 percent the total, either died with no clinical autopsy evidence of syphilis, or were livi from 3 to 40 years after infection with clinical evidence of the disease. Moreov 27.9 percent had a negative serologic test a were presumably cured.

[1]This chapter is a revision of the article *Studies in Syphilis.* VII. *The End Results of Untreated Syphilis,* which was published in the *Journal of Venereal Disease Information,* vol. 27, p. 293, 1946.

TABLE 35.—*Duration of syphilitic infection in 473 living and dead patients according to Bruusgaard*

Status of patient at last examination	Duration of infection in years								Total	
	3–10		10–20		20–30		30–40			
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
iving	79	25.6	66	21.3	100	32.4	64	20.7	309	100.0
ead	13	7.9	58	35.4	63	38.4	30	18.3	164	100.0
Total	92	19.4	124	26.2	163	34.5	94	19.9	473	100.0

However, these ratios tend to exaggerate ıe serious nature of the disease. Sowder (*35*), ıalyzing Brussgaard's material by several riteria of sampling, demonstrated that it vas weighted with cases showing the serious omplications of syphilis, and contained too ew patients who were symptom-free. Moreover, in the summarized tables presented ıerewith, many cases are included as syphiltic, even though the original data leave ome doubt as to the syphilitic etiology of heir disease. As an example of this type of veighting, cases showing "paralysis of the ıeart," "fatty heart," "arteriosclerosis," "organic heart lesion," and "cerebral apoplexy" ıre classified in this table as instances of cardiovascular syphilis, while cases of "epiepsy" and "psychosis" are included as cenral nervous system syphilis. Bruusgaard's observations, the only long-term study of the ınd results of untreated syphilis, appear to ndicate that, in terms of both morbidity and mortality, syphilis is not the dread disease it is commonly believed to be.

TABLE 36.—*Final diagnosis in 473 living and dead syphilitic patients according to Bruusgaard*

Final diagnosis	Living patients	Dead patients	Total	
			Number	Percent
Syphilis of central nervous system	[1] 31	6	[1] 37	7.8
Syphilis of cardiovascular system	[1] 21	48	[1] 69	14.6
Syphilis of skin and bone	58		58	12.2
Other syphilitic disease		3	3	.6
No evidence of syphilis, STS+	68		68	14.4
No evidence of syphilis, STS −	132		132	27.9
Cancer		29	29	6.1
Tuberculosis		29	29	6.1
Other disease		49	49	10.3
Total	[1] 310	164	[1] 474	100.0

[1] 1 duplication.

One other study (*30, 36, 37*) under the auspices of the United States Public Health Service, promises to be the most illuminating investigation of its type yet undertaken. The material, culled in Alabama from 1,782 male Negroes aged 25 or more who were serologically examined, included 399 syphilitic Negro males who had never received treatment, and 201 presumably nonsyphilitic Negro males. The untreated group all gave a history of infection and each had at least two positive serologic tests for syphilis. The first paper (*30*) presents a comparison between the morbidity rate in the untreated syphilitic patients and that observed in the nonsyphilitic Negroes. In the first group there were 46.6 percent with evidence of circulatory disease, as compared with 23.9 percent in the nonsyphilitic group. Also, 26.1 percent of the untreated syphilitic Negroes had either clinical or serologic evidence of central nervous system abnormalities, while only 2.5 percent of the nonsyphilitic group had any disease of this system. Finally, 12.5 percent of the untreated patients with syphilis presented evidence of disease of the bones, joints, and bursae. Information as to the duration of the disease in these patients at the time of their inclusion in the study is not given, but good evidence is presented to warrant the conclusion that morbidity in the untreated male Negroes with syphilis far exceeded that in a comparable presumably nonsyphilitic group.

These studies were extended in a later communication (*36*) dealing with the effect of the disease on the life span of the human host. The material on which this report was based was expanded to include 410 Negro men with untreated syphilis, in addition to the previously described group of 201 uninfected Negro men. Careful follow-up infor-

mation regarding these individuals was obtained since their original selection in the winters of 1931–32 and 1932–33, and it was felt that not one individual still living had been completely lost from observation. Through the end of 1944, 129 were known to have died, and 93 of these were examined post mortem. The study as reported was limited to the 12-year period between January 1, 1933, and December 31, 1944. Of the original group of 410 syphilitics, 101, or 24.6 percent, had died, as contrasted with only 28, or 13.9 percent, of the 201 controls. Life tables for the 2 groups were constructed and it was concluded that the life expectancy of the Negro man of age 25 to 50, infected with syphilis but untreated, was reduced on the average by about 20 percent. This investigation is still in progress, and subsequent publications dealing with the life cycle of the untreated disease, supplemented by the detailed post-mortem examinations that were conducted, will without doubt comprise an outstanding contribution to the literature, equaling if not exceeding in importance, the work of Bruusgaard.

These two studies employ different technics in their approach to the identical problem. Bruusgaard conducted clinical examinations on living patients, and surveyed the death records of deceased patients, all of whom at varying periods before had been classified as having early syphilis, and none of whom had received modern antisyphilitic therapy. The United States Public Health Service group is conducting continuing clinical studies, including autopsy investigations, on a carefully selected group of untreated early syphilis patients, information on whom can be expected to cumulate with the passage of time. The present report utilizes a third technic, heretofore not employed. All cases with historical, laboratory, or morphologic evidence of syphilis were selected from a large autopsy series, which has been described in previous chapters. The clinical record of each of these patients was reviewed and classified according to the kinds and amounts of therapy. The group of syphilitic patients for whom no evidence of therapy could be found is described in the present communication. This, then, is a retrospective study, and similar in this regard to the work of Bruusgaard. However, since the group was culled originally from an autopsy population, each individual in it was studied by post-mort examination.

Material

The 380 patients with syphilis who c stitute the basic material of this series reports are classified in table 37 according their treatment status. Of this entire gro 198 patients received no treatment for th disease with the following 11 exceptions received 2 bismuth injections, 3 receive bismuth injections, 2 received 4 bismuth jections, 1 received 5 bismuth injections, a 1 received mercury inunctions and potassi iodide by mouth for 6 weeks. All of th patients were considered to have been

TABLE 37.—*Treatment status of 380 syphilitic patients*

Treatment	Cases					
	No.	Percent	No.	Percent	No.	Per
Untreated	198	70.2	198	66.2	198	5
Inadequately treated[1]	72	25.5	72	24.1	72	1
Adequately treated[2]	12	4.3	12	4.0	12	
Total	282	100.0	.....	.....	.....	...
Treated but type and amount not known	.....	.....	17	5.7	17	
Total	.....	.....	299	100.0	.....	...
Unknown	.....	.....	.....	.....	81	2
Total	.....	.....	.....	.....	380	10

[1] Less than 20 arsenical and 20 heavy-metal injections
[2] 20 or more arsenical and 20 or more heavy-metal injecti

treated, and are so classified in the sub quent analysis. There were 129 males and females in this group of untreated syphil patients. The large majority, 150, were wh and the remaining 48 were Negroes. autopsy the central nervous system of 116 58.6 percent was examined.

It is evident from table 37 that in period under review from 1917 to 1941 majority of patients with syphilis who d and were autopsied at the New Haven H pital received no treatment for their disea Of those whose treatment status was know about three-quarters never were treated, wh only from 3 to 4 percent of the entire gro received adequate amounts of therapy acco ing to accepted standards prior to the int duction of rapid treatment methods or penicillin.

The duration of infection could be determined from the hospital records in only 37 the 198 cases. Of these, 18 were known to ve been infected for from 1 to 20 years, d 19 for from 21 to 30 or more years. cause of the relatively scant information ailable on this aspect of the study, it is not ssible to ascertain whether the time when fection occurred was in any way related to e absence of treatment. In table 38 is own the year of death and autopsy of the 8 patients. A large majority, 71.2 percent the total, were autopsied in 1927 or later, at is, 17 or more years after the discovery arsphenamine. Thus a considerable but known number of the group probably acired infections in the postarsphenamine riod.

ABLE 38.—*Year of death and autopsy of 198 untreated syphilitic patients*

Year	Patients	
	Number	Percent
17–21	29	14.7
22–26	28	14.1
27–31	43	21.7
32–36	53	26.8
37–41	45	22.7
Total	198	100.0

In table 39 are recorded the criteria for ne diagnosis of syphilis in the 198 untreated atients. Comparable values for the basic roup of 380 patients also are shown. This lassification is roughly arranged in decreasng order of clinical certainty of diagnosis. y positive anamnesis is meant a history of nfection, or a history of treatment of an infection, or a known previously positive serologic test for syphilis (STS) at some other clinic. In the final category of the table are placed a small number of patients never clinically diagnosed as syphilitic, but included because of the presence of specific anatomic changes at autopsy. The first three classes encompass 85 percent of the total untreated group, the diagnosis of syphilis in these patients having been based on historical evidence of infection together with a positive STS or spinal fluid, or significant lesions at autopsy.

Results

Table 40 summarizes the final status of the 198 untreated cases. Only 77 of this number, or 38.9 percent, presented any anatomic changes at autopsy consistent with a diagnosis of syphilis. In not all of these patients, however, was syphilis the primary cause of death. In less than half of those (31 patients, or 15.7 percent of the total) showing syphilitic lesions at autopsy, death occurred primarily as a result of some other disease. The majority of the 198 patients (121, or 61.1 percent) presented no evidence at autopsy of tissue alterations suggestive of syphilitic disease. In 80 of these, or 40.4 percent of the entire group, the serologic test for syphilis during the last hospital admission was positive, and 35 patients, or 17.7 percent of the total, had a negative STS on their last admission to the hospital. A final group of 6 patients with no anatomic evidence of syphilis had a doubtful or unknown STS.

TABLE 39.—*Criteria for diagnosis of syphilis in 198 untreated patients*

Description	Total cases		Untreated cases		Treated cases	
	Number	Percent	Number	Percent	Number	Percent
Positive anamnesis, positive STS or spinal fluid on last admission	213	56.1	127	64.1	86	47.3
Positive anamnesis, positive STS on previous admission	43	11.3	10	5.1	33	18.1
Positive anamnesis, no serologic or clinical evidence of syphilis on last admission but confirmation at autopsy by positive STS or presence of anatomic lesions	57	15.0	31	15.7	26	14.3
Positive anamnesis but doubtful STS on last admission	3	.8	1	.5	2	1.1
Positive anamnesis but no STS on last admission	15	3.9	5	2.5	10	5.5
Positive anamnesis but negative STS on last admission	38	10.0	23	11.6	15	8.2
Negative anamnesis, no STS on last admission, but anatomic lesions present at autopsy	11	2.9	1	.5	10	5.5
Total	380	100.0	198	100.0	182	100.0

TABLE 40.—*End results in 198 untreated syphilitic patients*

End result	Number		Percent	
Anatomic lesions present	77		38.9	
Primary cause of death		46		23.2
Subsidiary findings		31		15.7
Anatomic lesions absent	121		61.1	
STS positive		80		40.4
STS negative		35		17.7
STS doubtful or not known		6		3.0
Total	198	198	100.0	100.0

The anatomic lesions encountered at autopsy in the 77 patients with anatomic changes are tabulated in table 41. Of the 46 patients whose deaths were directly the result of syphilitic changes, 27 presented only one of the diagnostic categories listed in the table, 13 had two of these organic changes, and 6 had 3, with a total of 71 different recognizable syphilitic lesions. Of the 31 patients who died of some other disease process, but who had syphilitic lesions unrelated to the primary cause of death, 27 showed a single specific lesion, and 4 presented evidence of two different lesions. None in this group had three of the changes shown in table 41.

Discussion

A comparison of the Yale material that reported by Bruusgaard shows a rem able similarity between the two (table About 39 percent of our group of untr syphilitic patients were found at autops have anatomic evidence of syphilis, as trasted with Bruusgaard's finding of 35 cent with clinical or post-mortem or lesions of syphilis. In the Yale series 23 cent died primarily as a result of syph disease and Bruusgaard's population incl an identical ratio, 23 percent, with one o other of the serious end results of syp Conversely, in the Yale series 61 percent with no anatomic evidence of syphilis, Bruusgaard's group included 65 percent were living or who had died without indication of organic syphilis. The rati positive and negative serologic results in two groups is somewhat different, but perhaps may be accounted for by two fac (1) The large group in Bruusgaard's s whose STS was not known, and (2) differences which no doubt existed in

TABLE 41.—*Anatomic findings in 77 patients with untreated syphilis among whom 106 lesions were found at autopsy*

Type of lesion	Number of lesions found—			
	In 46 patients dying primarily of syphilis	In 31 patients with syphilitic changes a subsidiary finding	In all 77 pat	
			Number	P
Cardiovascular:				
Aortitis with or without valvulitis	26	29	55	
Aneurysm of arch	8	1	9	
Aneurysm of abdominal aorta	1	2	3	
Coronary arteritis	4	0	4	
Aortitis of leg vessels	3	0	3	
Cerebral arteritis	2	0	2	
Ruptured aneurysm of arch	9	0	9	
Ruptured aneurysm of innominate artery	1	0	1	
Ruptured cerebral aneurysm	2	0	2	
All cardiovascular	56	32	88	
Central nervous system:				
Tabes	2	1	3	
Meningitis	2	0	2	
Cerebral neurosyphilis	2	0	2	
Optic atrophy	0	1	1	
Total central nervous system	6	2	8	
Other types:				
Gumma of brain	1	0	1	
Gumma of heart	1	0	1	
Gumma of liver	3	0	3	
Gumma of testis	0	1	1	
Gumma of meninges	3	0	3	
Cirrhosis of liver	1	0	1	
Total other types	9	1	10	
Grand total	71	35	106	

TABLE 42.—*Summated comparison of end results of untreated syphilis in Bruusgaard's and the Yale series*

	Bruusgaard		Yale	
	Number	Percent	Number	Percent
Organic syphilitic disease	166	35.1	77	38.9
No evidence of syphilis, STS+	68	14.4	80	40.4
No evidence of syphilis, STS—	132	27.9	35	17.7
No evidence of syphilis, STS not known	107	22.6	6	3.0
Total	473	100.0	198	100.0

sensitivity of the serologic tests employed in the two series.

From table 41 it is seen that only about 8 percent of the Yale group presented any evidence of syphilitic disease of the central nervous system. A post-mortem examination of the central nervous system is not a routine procedure in our laboratory. If it were, perhaps a larger number of patients with central nervous system involvement might have been found, and this in turn would have increased the proportion of poor end results. This possibility cannot of course be dismissed lightly. However, there are two factors that should be considered. In the first place it has been a practice to make special efforts to obtain permission for an examination of the central nervous system whenever clinical signs suggest involvement of this system. Furthermore, as shown in table 43, of 116 patients whose autopsy examination included a study of the central nervous system, 47, or 40.5 percent, had anatomic evidence of syphilitic disease. This value does not differ significantly from the 36.6 percent of the 82 patients who did not have post-mortem examinations of the central nervous system but who did show anatomic lesions of other organs. The two groups show no evidence of heterogeneity with respect to the presence or absence of anatomic lesions and this suggests that the failure to examine the central nervous system in all cases may not have materially influenced the result.

Sowder has shown that Bruusgaard's data are weighted to emphasize the more serious complications of the disease. The Yale material may be subject to the opposite criticism that, particularly as regards central nervous system syphilis, it is weighted in favor of the less serious end results of syphilis. The New Haven Hospital, a general hospital for acute diseases does not make a practice of admitting the deteriorated patient with central nervous system syphilis. These patients ultimately reach the various State hospitals, and to this extent our material is biased. We have no method of evaluating the influence of this sampling error on our end results, but the general agreement between our findings and those of Bruusgaard suggests that it is not excessive.

If it is assumed that our findings represent a fairly accurate summary of the end results of untreated syphilis, it can be concluded that had treatment been administered adequately and early to the entire group it could not possibly have effectively altered the course of the disease in more than 4 out of 10 patients, since 6 out of 10 untreated patients died with no evidence of syphilis at autopsy. On closer inspection even this ratio of 4 out of 10 patients who could have benefited by treatment is excessive, because only a little more than 2 out of 10 actually died as a result of syphilis. The remaining 8 out of 10 patients with syphilis all succumbed to an unrelated disease process, and the fact that some of them had developed a syphilitic lesion, or a positive STS, was apparently of no great significance. Treatment of the whole group could then have possibly altered the

TABLE 43.—*Presence or absence of anatomic lesions of syphilis in patients with and without post-mortem examination of central nervous system*

	C N S examined		C N S not examined		Total	
	Number	Percent	Number	Percent	Number	Percent
Anatomic lesions present	47	40.5	30	36.6	77	38.9
Anatomic lesions absent	69	59.5	52	63.4	121	61.1
Total	116	100.0	82	100.0	198	100.0

end result in only the 2 who actually died of syphilis out of 10 untreated cases.

This conclusion, however, does not place proper emphasis on the fact that syphilis is a dynamic disease, static at some times, progressive and developing at others. Certainly an unknown number of the group with incidental syphilitic lesions at autopsy would have died of syphilis had they survived the illness to which they finally succumbed. Some of these syphilitic lesions, if given time to develop, would have progressed to a stage where death would have resulted. Furthermore, the real significance of a positive STS in the absence of anatomic lesions is not fully understood. No doubt the serologic findings in some of these instances reflect the immune state of the host, but in others it may very well represent the reaction to tissue changes unrecognizable by known technics. Insofar as the latter hypothesis is correct, a positive STS may indicate an early phase of a reactive process which, provided the patient lives long enough, ultimately develops into a recognizable anatomic lesion. The value of antisyphilitic treatment should therefore not be gaged in the limited terms of the 2 out of 10 in the Yale group who died of syphilis. Rather is the value of syphilis therapy directly related to the over-all efforts to prolong life by reducing the mortality from other diseases. Every syphilitic patient saved by sulfonamide preparations or penicillin from death due to pneumonia, or appendiceal abscess, or meningitis, or streptococcic infections, becomes liable to death from syphilis. Every syphilitic patient with malignant disease, or traumatic injuries, or hypertension who is cured by surgical intervention becomes ultimately susceptible to death from syphilis. Viewed in this light the prompt and adequate treatment of patients with syphilis becomes a life-saving measure out of all proportion to the 2 in 10 ratio which in this study was the actual death rate from untreated syphilis.

The above statements have emphasized mortality as a direct result of syphilitic inf tion and have failed to give proper weig to the influence of syphilis on host susc tibility to other diseases. Definitive inform tion on this point is not available, but preliminary study of the autopsy data fr Alabama (37) gives the impression that t great difference in mortality rates between t syphilitic and control groups in that inves gation was due as much to other diseases to syphilis itself. This suggests that many m have succumbed to an intercurrent disea more easily because of syphilitic infecti This impression is corroborated by the rec study of Deibert and M. C. Bruyere (38 which shows that there is greater morbid present among untreated syphilitics th among nonsyphilitics, even in areas not co monly associated with syphilis. It is appare that a case fatality rate of at least 20 perce is ample justification for the most strenuo efforts to provide prompt and adequate tre ment of all cases. This is the more true sin fatalities due to syphilis usually follow lo periods of disability. Even when not fat there is evidence to suggest that syphi probably lowers life expectancy significant

Nevertheless the evidence at hand does dicate that syphilis is occasionally a se limited disease. In the Yale material the were 35 patients (17.7 percent of the to syphilitic group) with a negative STS duri their last hospital stay, and with comple absence of anatomic evidence of syphilis autopsy. From all indications these patie were spontaneously cured, demonstrating th a certain proportion of individuals poss adequate defense mechanisms which c counteract syphilitic infection and complete eliminate any morphologic evidence of t disease. The exact nature of these defen factors is not known but their sum total encompassed in the general term "host sistance." The recognition that host resistan to syphilis does exist should serve as impetus to studies in this field.

RÉSUMÉ AND RECOMMENDATIONS

A review of the available literature on the incidence of morphologic evidence of syphilis in autopsies on adults revealed widely different rates, varying from a low of 2.6 percent to a high of 29.5 percent. The factors which might have contributed to these different results were subjected to critical analysis. On the basis of these reports, it was established that lesions of syphilis were more frequently observed in the Negro race than in the white, and that they were likewise more frequent in males than in females, but it could not be demonstrated conclusively that these factors were responsible for the divergent estimates of the incidence of syphilis at autopsy. The great variability in diagnostic criteria, both gross and microscopic, employed by different investigators was appraised, and it was concluded that it was this lack of uniformity in diagnostic criteria which was the major factor responsible for the widely diverse findings reported in the literature.

These observations initiated a survey of the Yale material, which had as its purpose the study of many of the problems not heretofore clarified in reports on syphilis at autopsy. From September 22, 1917, to March 8, 1941, 5,300 autopsies were performed at the Yale University School of Medicine. Of these 3,907 were upon individuals aged 20 or over, and of this number, 380, or 9.7 percent, had clinical or laboratory or postmortem evidence of syphilis. The method employed in selecting two control groups from the nonsyphilitic population for further comparison with this syphilitic group was described, and it was demonstrated that these two control groups represent random samples from the total nonsyphilitic population as regards age, sex, and race. The punch-card code which was utilized in all subsequent analyses of this material was also presented.

The highest rates for syphilis at autopsy were reported by investigators who accepted Warthin's criteria of fibrosis and round cell infiltration for the morphologic diagnosis of syphilis. The lowest rates, on the other hand, were observed by those who either antedated Warthin or did not adopt his teachings. Clearly here was a problem which could be clarified by a study of the Yale material. To accomplish this purpose, microscopic preparations of the heart, liver, pancreas, adrenals, and testes from 283 syphilitic and 722 nonsyphilitic white persons were studied with respect to the frequency of Warthin lesions. No qualitative differences could be discerned between the fibroid and cellular changes observed in the organs of syphilitic persons and those of the nonsyphilitic controls. The two groups did not differ significantly when they were compared with respect to the incidence of Warthin lesions in the heart, liver, adrenals, and testes. Pancreatic lesions were probably significantly more frequent among syphilitics than among nonsyphilitic persons, but no explanation could be found for the relatively high frequency of these changes in the latter group. The group of syphilitic persons was divided into two categories, those with and those without frank anatomic alterations characteristic of syphilitic infection, and the incidence of Warthin lesions of the five parenchymatous organs in the two subgroups was compared. In no instance was a significant difference found. Finally an analysis of the age distribution of persons with and without Warthin changes indicated that the aging process is related to the presence of these lesions. On the basis of these findings it was concluded that the evidence did not support the concept that the microscopic changes described by Warthin are pathognomonic of syphilitic infection.

The Yale autopsy material was studied for information on morbidity and mortality rates and the variables affecting these rates. Of the

3,907 individuals over 20 years of age who were autopsied in the period under review, 380 had clinical or laboratory or anatomic evidence of syphilis. This represents 9.7 percent of the population, and confirms the statement that "syphilis strikes 1 out of 10 adults." In this group of syphilitics were 156 individuals, or 41 percent, with morphologic lesions of syphilis, and 90, or 57.7 percent, of these died primarily as a result of their syphilis. In this experience 3 out of 10 persons with clinically diagnosed syphilis developed significant tissue lesions, and 1 out of 5 died therefrom. A summation of three different autopsy populations, one of which was the Yale material, disclosed that syphilitic lesions at autopsy were from two to four times as frequent in the Negro as in the white. Nevertheless, the syphilitic Negro appeared no more likely to develop a tissue lesion recognizable at autopsy and had no greater chance of dying therefrom than the white syphilitic. The mean age at death of syphilitic and nonsyphilitic Negroes was identical, but both of these groups died at a significantly earlier mean age than whites of comparable categories. This observation suggests that the shorter life expectancy of Negroes as contrasted to whites may be due not to the greater frequency of syphilis among Negroes, but rather to nonspecific social and economic influences which adversely affect their life span.

In the Yale series, syphilitic males with lesions at autopsy comprised 4.7 percent of the male population and syphilitic females with lesions constituted 2.7 percent of the female population. These two values are significantly different. Sex, therefore, appeared to exert a definite influence on resistance to the tissue changes of late syphilis, and this was independent of race.

In a consideration of the white individuals examined at autopsy in the Yale series, no significant differences were found among the mean ages at death of any of the following groups: Nonsyphilitic controls, syphilitics with anatomic lesions, syphilitics without anatomic lesions, syphilitics dying primarily of the disease, syphilitics with anatomic lesions of syphilis who died of an unrelated disease process. All of these groups had a mean age at death of approximately 53 years. However, a significantly higher percentage of deaths occurred among syphiliti in the age group 40 to 70 years than amor nonsyphilitics. Moreover, although about 2 percent of nonsyphilitics survived age 7 only about 10 percent of syphilitics survive this age. This was true not only for th syphilitics with lesions at autopsy, but als for those without anatomic lesions. Fro these findings the conclusion was reached th the mere fact of syphilitic infection si nificantly reduces longevity, regardless whether or not tissue lesions result.

Of the 380 syphilitics comprising the Ya material, 197 had positive and 116 negati serologic tests on their last hospital admi sion. A study of this combined group of 31 cases resulted in the following conclusion

1. Serologic positivity was signi cantly more frequently associated wi anatomic lesions than was serologic ne ativity.

2. Approximately one-quarter of a syphilitics with specific anatomic lesio at autopsy were serologically negative o their last admission.

3. Approximately one-half of a individuals with positive serologic tes showed no anatomic changes consiste with a diagnosis of syphilis at autopsy.

4. In patients with positive serolog tests, the presence of anatomic lesio was diagnosed correctly in about thre fourths of the cases. About one-fifth o all patients with positive tests as the on indication of infection had organic l sions of syphilis at autopsy, and syphil was primarily responsible for the dea of 1 in 20.

5. In syphilitic individuals with ne ative serologic tests, a clinical evaluatio leading to a specifically stated impre sion of "no anatomic lesion" or "cure was likely to be no more accurate whe checked with findings at autopsy than clinical diagnosis of organic disease.

6. About four-fifths of the syphiliti who died primarily as the result of o ganic syphilitic disease had positive ser logic tests. The frequency of positiv tests in this group was greater than i the group with anatomic lesions of syp ilis an incidental finding at autops

while the group with no lesions at autopsy had the lowest proportion of positive tests. This suggests that increasing activity of the disease is associated with an increasing frequency of positive blood tests.

7. Syphilitic organic disease was primarily responsible for the death of about one-quarter of all cases with positive and about one-tenth of those with negative serologic tests. The likelihood of syphilis being the primary cause of death was more than twice as great in individuals with positive as in syphilitics with negative serologic tests.

8. Anatomic changes of syphilis were observed in about one-sixth of those in whom serologic reversal had occurred.

9. Sex did not influence the incidence of positive or negative serologic tests among individuals with syphilitic lesions at autopsy or the frequency of syphilitic lesions as a primary cause of death.

In view of Warthin's reports on the tissue anges which he interpreted as pathognonic of syphilitic infection, the relation of ese lesions to the results of serologic tests r syphilis was investigated. Two groups of philitic individuals, one group with positive d the other with negative serums, were mpared as to the frequency of the Warthin anges in each of five parenchymatous orns. Organ for organ, the incidence of these sions in the two groups was not significntly different. Moreover, syphilitic persons ith typical Warthin lesions in multiple orns were no more likely to present serologic idence of syphilis than were those with Varthin lesions in only one organ. On the sis of these findings, it was concluded that e changes described by Warthin are not lated to the reaction of the serum to known sts for syphilis.

Of the 380 syphilitic patients who are scribed in this series of reports, 198, or 2.1 percent, received no specific therapy. A udy of this group was made in order to etermine the distribution of morphologic sions of syphilis in an untreated syphilitic opulation. Anatomic lesions of syphilis were und in 77, or 38.9 percent, of these untreated patients, but only 23.2 percent of the entire group died primarily as a result of syphilis. One hundred and six different lesions were found in these 77 syphilitics; 88 (83.0 percent) occurring in the cardiovascular system, and 8 (7.6 percent) occurring in the central nervous system. The remainder (10, or 9.4 percent) were gummatous lesions of various organs, and cirrhosis of the liver. Anatomic lesions of syphilis were absent in 121 patients (61.1 percent). In 80 (40.4 percent), the blood serologic test during the last hospital stay was positive, and in 35 (17.7 percent) it was negative. From these findings it appears that untreated syphilis in this series had a case fatality rate of about 1 in 5, and a spontaneous cure rate also of about 1 in 5. There was a close parallelism between these observations and those reported by Bruusgaard.

Recommendations

With the completion of this series of reports, it is apparent that two serious deficiencies must be overcome if future studies of a similar nature are to prove worth while.

Anatomic Criteria for Diagnosis of Syphilis

The first chapter has emphasized the widely different criteria employed in different laboratories of pathology for the anatomic diagnosis of syphilis. Until uniform criteria are generally adopted and consistently followed in the large teaching centers, it is improbable that any definitive understanding of the anatomy of the disease syphilis will result. In order to overcome this obstacle to a comprehension of the basic disease process, it is suggested that a committee of pathologists be organized under the auspices of the United States Public Health Service to consider the entire question of the morphologic criteria for a diagnosis of syphilis. Such a committee should be aided by the establishment of a registry of anatomic syphilis, to which pathologists from all over the country would be invited to contribute material for diagnosis and study. On the basis of continuing studies, the committee would present its conclusions in a series of authoritative and comprehensive recommendations. These would no doubt be

readily accepted by the profession in general and by pathologists in particular. Thus one of the pitfalls to our understanding of the disease would be eliminated.

Inadequacy of Sample

Autopsies conducted over a period of a quarter of a century at the Yale School of Medicine produced only a handful of syphilis cases, 380 in number, for study in these reports. Again and again, as indicated in the text, this group proved to be an inadequate sample from which to draw conclusions. At least two important originally contemplated studies were of necessity abandoned because of the inadequacy of our sample. These were: (1) an evaluation of the influence of syphilis on host susceptibility or resistance to other disease processes, and (2) a survey of the end results of adequately treated syphilis. Neither of these subjects has to date been studied on the basis of autopsy materia the autopsy protocols of other institu were pooled with our own, a reservoi information would soon be available which would flow many of the answe the vexing questions posed in the bod these reports. Such a cooperative enter could be formally organized under the pices of the United States Public H Service. The pattern of procedure uti with such success by the Penicillin Pan the National Research Council in stu the effectiveness of penicillin in the ment of syphilis could readily be util This proposal envisages the organization Central Statistical Bureau for the coding punch carding of autopsy protocols subm by participating institutions. In this ma a mass of data would soon become avai which could serve as the basis for the inv gation not only of syphilis, but also of r other morbid processes.

APPENDIX

Code for Syphilis Survey

olumn	*Description*
1–4	Autopsy number
5–6	Year of autopsy
7–8	Month of death
9–10	Type of autopsy 1 Thorax 2 Abdomen 4 Head 8 Spinal cord 16 Neck organs 32 Extremities (Code sum)
11	Hospital and service 1 New Haven—Medical 2 New Haven—Surgical 3 New Haven—Maternity—mother 4 New Haven—Maternity—infant 5 New Haven—Other 6 Outside doctor—No hospital admission 7 Outside tuberculosis hospital 8 Outside—Other than tuberculosis hospital 9 Medical examiner or coroner (in or out hospital) 0 Sudden death
12	Reserved for expansion
13	Clinical status last admission 0 Cured—Negative Wassermann and no clinical evidence 1 Latent—Only evidence is positive Wassermann 2 Cardiovascular syphilis 3 Central nervous system syphilis 4 Cardiovascular plus central nervous system 5 Other than cardiovascular or central nervous system 6 Cardiovascular plus other than central nervous system 7 Central nervous system plus other than cardiovascular 8 Cardiovascular plus central nervous system plus other 9 No serological or clinical evidence of syphilis, but positive past history overlooked on last admission
14–15	Age in years—Age known Code years

Column	*Description*
16	Age in years—Age not known but estimated 2—20 to 29 years 3—30 to 39 years 4—40 to 49 years 5—50 to 59 years 6—60 to 69 years 7—70 to 79 years 8—80+
17	Sex 1 male 2 female 3 not known
18	Marital status 1 unmarried 2 marital status unknown 3 married, widower, or divorced (males only) 4 married, nulliparous 5 married, parous 6 married, gravidity unknown
19	Nativity 0 United States 1 England, Ireland, Scotland, and Wales 2 Europe, except Russia and Slavs and Scandinavians 3 Russia and Slavs (Jugo, Czechs, Poland, Bulgaria) 4 Scandinavia 5 Latin America, South America 6 Asiatic 7 All others 8 Unknown
20	Color 0 unknown 1 white 2 black 3 yellow 4 all others
21	Occupation 0 unknown 1 housewife 2 laborer unclassified 3 trades 4 personal service and clerical 5 transportation 6 profession and skilled trades 7 all other employed 8 school 9 unemployed (includes women)

Column	Description
22	History of early syphilis—Personal 0 no history or unknown 1 primary genital lesion 2 primary extragenital lesion 3 secondary 4 primary and secondary
23	History of late syphilis 0 unknown or no history 1 cardiovascular 2 central nervous system 4 other, including positive serology (Punch sum)
24	History of syphilis, familial 0 unknown or no history 1 spouse with syphilis 2 offspring with syphilis 4 siblings with syphilis (Punch sum)
25	Diagnosis of syphilis 1 ante mortem 2 post mortem 3 ante mortem and post mortem 4 not diagnosed either ante or post mortem
26	Diseases diagnosed ante mortem 1 diabetes 2 Buerger's disease (Punch sum)
27	Serology—Ante-mortem Wassermann, alcohol, or cholesterol antigen 0 unknown or not done 1 negative 2 doubtful 3 positive Last admission 4 previously positive but negative on last admission (± or + = doubtful. If two tests are performed, err in favor of positivity.)
28	Serology—Ante-mortem Kahn Same as column 27
29	Serology—Ante mortem, other than Kahn or Wassermann Same as column 27
30	Serology—Post mortem, any test Same as column 27
31–32	Spinal Fluid 00 unknown or not done 0 all negative 1 abnormal sugar—below 45 or above 85 2 abnormal protein—more than 45 4 increased w. b. c.—more than 8 8 r. b. c. present 16 serology positive 32 colloidal gold—abnormal (Punch sum)
33	Darkfield examination 0 performed but results not known 1 not done 2 negative and doubtful 3 positive
34	Blood pressure—systolic 0—not known 1—under 99 2—100–139 3—140–199 4—over 200
35	Blood pressure—diastolic 0—not known 1—under 50 2—under 75 3—75–99 4—100–124 5—over 125
36	Duration of disease 0—less than 1 year 1—1 to 5 years 2—6 to 10 years 3—11 to 15 years 4—16 to 20 years 5—21 to 25 years 6—26 to 30 years 7—over 30 years 8—unknown
37	Treatment—Arsenical (trivalent) 0—unknown 1—no treatment 2—less than 10 injections 3—10 to 19 injections 4—20 or more 5—received, but number not known
38	Spacing of treatment—arsenical 0 not known 1 continuous 2 discontinuous
39	Stage of disease at first arsenical 0 unknown 1 seronegative primary 2 seropositive primary 3 sero-unknown primary 4 secondary 5 latent syphilis (after 2 years) 6 tertiary (with lesion)

Column	Description
))	Treatment—Heavy metal Same as column 37
1	Stage of disease at first heavy metal Same as column 39
2–43	Other treatment 1 treatment given but character or amount unknown 2 tryparsamide 4 hyperpyrexia 8 other (Punch sum)
4	Post-mortem diagnosis of syphilis 1 gross with no microscopic confirmation 2 gross with microscopic confirmation 3 microscopic with no gross confirmation
45	Microscopic fibrosis and/or round cells in testicle 0 slide absent 1 no increased fibrosis or round cells 2 minimal, 3 intermediate, 4 maximal } fibrosis of interstitium and round cells plus tubular atrophy 5 — 6 — 7 — 8 other pathological process obscuring picture
46	Microscopic fibrosis and/or round cells in liver 0 slide absent 1 minimal, 2 intermediate, 3 maximal } fibrosis with round cell infiltration 4 no increased fibrosis but round cells present 5 no fibrosis and no round cells 6 other pathological process obscuring picture
47	Microscopic fibrosis and/or round cells in pancreas Same as column 46
48	Microscopic fibrosis and/or round cells in adrenal 0 slide absent 1 no increase in fibrosis or round cells 2 minimal, 3 intermediate, 4 maximal } round cells without fibrosis 5 — 6 — 7 —
49	Microscopic fibrosis and/or round cells in heart 0 slide absent 1 no increase in fibrosis and no round cells 2 minimal, 3 intermediate, 4 maximal } fibrosis with round cell infiltration 5 — 6 — 7 — 8 other pathological process obscuring picture
50–51	Heart weight in decigrams 00 no weight or not recorded
52	Coronary arteries 0 not examined or unknown 1 essentially normal 2 narrowed moderately 3 narrowed markedly 4 occluded
53–54	Treatment reaction 1 dermatitis 2 purpura 4 encephalitis 8 jaundice 16 aplastic anemia 32 any other (Punch sum)
55	Experimental or control group 1 experimental 2 control group A 3 control group B
56	Number of cards for case
57–58	Reserved for expansion
59	Syphilis at autopsy 1 syphilis primary cause of death 2 syphilis incidental finding 3 syphilis not evident at autopsy
60	Other anatomical findings 1 disease of gallbladder 2 disease of prostate 4 disease of fallopian tubes (Code sum)
61–67	Principal primary autopsy diagnosis (Primary cause of death)
68–74	Subsidiary disease process at autopsy
75–78	Syphilis at autopsy
79	Reserved for expansion
80	Card number of case

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